INTERNATIONAL SEARCH REPORT

Im[redacted]l Application No
PCT/IN 00/00023

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
CHEM ABS Data, EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CHEMICAL ABSTRACTS, vol. 109, no. 25, 19 December 1988 (1988-12-19) Columbus, Ohio, US; abstract no. 223418, REN, CAIYUAN ET AL: "Image-forming contraceptive for blocking of oviducts or vas deferens" XP002143456 abstract & CN 85 108 504 A (NORTHWEST UNIVERSITY, PEOP. REP. CHINA) 20 May 1987 (1987-05-20) ---	1,3,5, 15-22
A	GB 1 569 660 A (MEDLINE AB) 18 June 1980 (1980-06-18) the whole document ---	1-29
	-/--	

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 July 2000	10/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Boulois, D

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Int. [redacted] Application No
PCT/IN 00/00023

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	US 5 488 075 A (GUHA SUJOY K) 30 January 1996 (1996-01-30) claims	1-29
A	US 4 040 417 A (ZIPPER JAIME A) 9 August 1977 (1977-08-09) claims	1-29
A	US 4 185 618 A (COREY HAROLD) 29 January 1980 (1980-01-29) column 1, line 56 -column 3, line 16	1-29

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No
PCT/IN 00/00023

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
CN 85108504 A		NONE	
GB 1569660 A	18-06-1980	IN 148540 A	28-03-1981
		SE 7608618 A	01-02-1978
US 5488075 A	30-01-1996	NONE	
US 4040417 A	09-08-1977	US 3803308 A	09-04-1974
US 4185618 A	29-01-1980	CA 1046405 A	16-01-1979
		DE 2700190 A	14-07-1977
		FR 2336945 A	29-07-1977
		GB 1554783 A	31-10-1979
		JP 52087238 A	20-07-1977
		NL 7614190 A	07-07-1977

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
IN/PA267/SKG		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/IN 00/ 00023	16/03/2000	17/03/1999
Applicant		
GUHA, Sujoy, Kumar		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   [ ] the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   [ ] contained in the international application in written form.

   [ ] filed together with the international application in computer readable form.

   [ ] furnished subsequently to this Authority in written form.

   [ ] furnished subsequently to this Authority in computer readble form.

   [ ] the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   [ ] the statement that the information recorded in computer readable form is identical to the written sequence listing has be n furnished

2. [ ] **Certain claims were found unsearchable** (See Box I).

3. [ ] **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract,**

   [X] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within on month from the date of mailing of this international search report, submit comments to this Authority.

6. Th figure of th **drawing** to be publish d with th abstract is Figure No. —

   [ ] as suggested by the applicant.

   [ ] because th applicant failed to suggest a figure.

   [ ] because this figure better characterizes th inv ntion.

   [ ] Non of the figures.

INTERNATIONAL SEARCH REPORT

International Application No
P[illegible]IN 00/00023

A. CLASSIFICATION OF SUBJECT MATTE
IPC 7 A61K9/10

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CHEM ABS Data, EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 July 2000	10/08/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Boulois, D

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/IN 00/00023

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/IN 00/00023

Patent document cited in search report	Publication dat	Patent family member(s)	Publication dat
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GB 1569660 A	18-06-1980	IN 148540 A SE 7608618 A	28-03-1981 01-02-1978
US 5488075 A	30-01-1996	NONE	
US 4040417 A	09-08-1977	US 3803308 A	09-04-1974
US 4185618 A	29-01-1980	CA 1046405 A DE 2700190 A FR 2336945 A GB 1554783 A JP 52087238 A NL 7614190 A	16-01-1979 14-07-1977 29-07-1977 31-10-1979 20-07-1977 07-07-1977

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

WRITTEN OPINION

(PCT Rule 66)

To:
MEHTA, Ramesh, Kumar
REMFRY & SAGAR
Attorneys-at-Law
Remfry House
8, Nangal Raya business centre
New Delhi, IN-110046
INDE

Date of mailing *(day/month/year)* 27.12.2000

REPLY DUE **within 3 month(s)** from the above date of mailing 27.3.20

Applicant's or agent's file reference
IN/PA267/SKG

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IN00/00023	16/03/2000	17/03/1999

International Patent Classification (IPC) or both national classification and IPC
A61K9/10

Applicant
GUHA, Sujoy, Kumar

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 17/07/2001.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
Hedegaard, A

Formalities officer (incl. extension of time limits)
Götz, K
Telephone No. +49 89 2399 7381

I. Basis of the opinion

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

Description, pages:

1-19	as originally filed

Claims, No.:

1-8	as originally filed
9-20,23-29	as amended under Article 19

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 20,29,

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 20,29 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrialapplicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-19 No
Inventive step (IS)	Claims	23-28 No
Industrial applicability (IA)	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Section III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Due to the feature "substantially described herein above" the wording of claims 20 and 29 is such that a meaningful opinion cannot be formed. Said claims should be deleted.

Re Section V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

   D1: Chemical abstracts, vol. 109, no. 25 (1988-12-19) abstract no. 223418

2. The subject-matter of claim 1 is not novel (Art. 33(2) PCT) over D1, which discloses a contraceptive comprising nylon (contraceptive polymer), ethanol (a solvent medium) and Cu-Zn alloys (an electrically conducting material and magnetic material).

   It is pointed out that due to the use of the term "preferable" several times in claim 1 the characterising portion of said claim cannot render the subject-matter novel over D1. It appears necessary to delete said term.

3. The subject-matter of claims 23-28 is novel since a process according to independent claim 23 comprising the steps of dissolving styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in a solvent medium, followed by keeping the complex solution of said copolymer in an inert environment and shaking for 45-50 hrs by maintaining the temperature at 35°C has not been disclosed in any of the available prior art documents.

4. Concerning inventive step (Art. 33(3) PCT) it is pointed out that D1 (closest prior art) already has disclosed the advantage of providing contraceptives comprising polymers and which can be controlled and verified after insertion. Hence, in the absence of any unexpected effects with respect to D1 the subject-matter of claim 23 is not considered to involve an inventive step.

5. A positive international preliminary report for the subject-matter of the dependent claims 2-19 and 24-28 can only be established when they refer to independent claims which meet the requirements of the PCT.

Re Section VII

Certain defects in the international application

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1 is not mentioned in the description, nor is this document identified therein.

Re Section VIII

Certain observations on the international application

1. The words "about", "approximately" and "improved" detract from the general clarity and should be deleted throughout the claims (Art. 6 PCT).

2. The phrase "not intended to restrict/limit the scope of the invention" (see p. 12, l. 29-30 and p. 17, l. 25) is vague and unnecessary and should be deleted (Art. 6 PCT).

3. The description must be brought into conformity with the new claims to be filed; care should be taken during revision not to add subject-matter which extends beyond the content of the application as originally filed; Article 34.2 b) PCT.

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TX 523 656 epmu d
FAX +49 89 2399-4465

Correspondence with the EPO on PCT Chapter II demands

In order to ensure that your PCT Chapter II demand is dealt with as promptly as possible you are requested to use the enclosed self-adhesive labels with any correspondence relating to the demand sent to the Munich Office.

One of these labels should be affixed to a prominent place in the upper part of the letter or form etc. which you are filing.

retrograde actum on the ovary in the female, which reduces the chance of actual fertility restoration even when by surgery the device is removed or replaced by another such device for restoring fertility. Still another disadvantage of such known devices is that the insertion into the urethra of some of such devices either permanently, till desired by the patient or temporarily, for each act of intercourse, is painful and likely to produce erosion and infection. Yet another disadvantage of such known devices is that the use of some of such devices requires attention of the user prior and after such intercourse. Further disadvantage associated with such known devices is that the large size of some of such devices leads to rupture of the vas deferens in many cases. Still further disadvantage associated with such known devices is that the use of some of such devices totally destroys a segment of the vas deferens and/or fallopian tube, hence reversal would require special microsurgery to rejoin the vas deferens and/or fallopian tube. Yet further disadvantage associated with such known devices is that the removal of some of such devices becomes difficult and calls for a complicated procedure on account of fibrosis with low success rate.

Yet another class of occlusion methods to achieve contraception or sterilization includes formation of a chemical preparation based plug in the vas deferens and/or fallopian tube, such as formation of polyurethane plug (*UK Patent no. GB2223025*) or neem oil plug (*US Patent no. 5,501,855*) or styrene maleic anhydride copolymer plug (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The polyurethane plug is formed by reacting pre-polymer of polyurethane with a chain-enlargement agent with amino-group under normal atmospheric temperature or above it in the presence of an organic solvent and organic acid catalyst, which is solidified in the ductus deferens (*UK Patent no. GB2223025*). The reversibility is achieved by removal of the plug. The neem oil plug is formed by intra-vas administration of neem oil to male rats, which resulted in blockage of spermatogenesis without affecting the testosterone production (*US Patent no. 5,501,855*). The reversibility has not been achieved. The styrene maleic anhydride copolymer plug is formed by step irradiation of styrene maleic anhydride at a dose of 0.2 to 0.24 megarad for its every 40 gms followed by dissolution in pure dimethyl sulphoxide and thereafter injected into the lumen of the vas deferens (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The reversibility is achieved by flushing of the styrene maleic anhydride copolymer plug by injecting extra dose of pure dimethyl sulphoxide.

The polyurethane plug suffers from similar disadvantages as that of the contraceptive devices for use by male or by male and female, as described herein above.

The neem oil plug preparation has limitation that, it does not polymerise rapidly after injection and hence travels retrograde into the testes. Further, it causes damages to the testes and testicular size reduces. Still further disadvantage of neem oil plug is that the lymph nodes are affected. Yet another limitation of the neem oil plug is that the restoration of fertility is not possible.

The styrene maleic anhydride copolymer plug, herein after referred to as SMA plug, which is undergoing multicentric Phase-III Clinical Trials in India and has been developed by the inventor of the presently disclosed invention, has been observed to have certain limitations, such as, it cannot be detected and/or suitably quantified externally by means of X-ray, CAT scanning, magnetic resonance imaging (MRI) or magnetic field due to the non-radio-opaque nature of the contraceptive drug. Another limitation of SMA plug is that, its spread or distribution in the reproductive tract after injection cannot be controlled. Further limitation of SMA plug is that, for its removal to restore the fertility, another injection of extra dose of dimethyl sulphoxide is required to be given to the patient, hence it cannot be removed from the body conveniently by non-invasive and external means except by using the reversal device disclosed in the *pending Indian Patent application no. 928/DEL/97*, developed by inventor of the present invention. However, the removal of the contraceptive even by this device is not 100% successful due to the difficulty in removal of the contraceptive from the part of vas deferens leading to the prostate region.

The limitations of SMA plug, as described herein above, have also been observed in other similar contraceptive preparations, such as polyurethane plug, neem oil etc., which are intended to be used by male or female or male and female for blockage of the vas deferens and/or fallopian tube by way of formation of plug or for affecting the nature of sperm and/or ovum for achieving the contraception or sterilization, as the basic compound of the such known contraceptive preparations being non-radio-opaque and non-magnetic in character. The MRI also fails to detect the contraceptive mainly due to its poor contrast with the soft tissue. The ultrasound is also incapable of detecting the contraceptive, due to low percentage of the basic compound and inadequate difference of the characteristic impedance from the body tissue. To overcome this disadvantage, if the net percentage of the basic compound is increased, it will have the disadvantages

This is further an object of this invention to disclose a contraceptive which necessarily does not require any surgery or flushing of any solvent for its removal from the reproductive duct to restore the fertility and can be removed from the body by non-invasive and external means.

This is still an object of this invention to disclose a contraceptive, which is required to be injected only once for achieving contraception.

This is yet an object of this invention to disclose a contraceptive which can be reversed by external non-invasive means and necessarily does not require additional injection of an extra dose of the pure solvent, thus avoid the second injection.

This is still further an object of this invention to disclose a contraceptive which not only acts as a blocking agent but also brings about changes in the sperm and/or ovum to result in the contraceptive action, hence overcome the disadvantages associated with the contraceptives capable of acting as blocking agent alone.

Brief Description and Preferred Embodiments of the Invention :-

Accordingly this invention provides a complete disclosure of an improved injectable reversible contraceptive and the method of preparation and use thereof, having above stated characteristics and consisting of contraceptive polymer, a solvent medium, an electrically conducting material and magnetic material, characterised in that the contraceptive polymer is preferably from the hydrogel class of polymers, more preferably a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and the solvent medium is preferably dimethyl sulphoxide solvent, and the electrically conducting material and the magnetic material are essentially taken in the particle forms of microsize and macrosize, particularly it discloses a contraceptive consisting of contraceptive polymer having electrical charge and pH lowering properties, a solvent medium having complexing properties, an electrically conducting material having charge transfer, sperm membrane and ovum covering molecule exchange, and inductive heating properties and magnetic material having magnetising and magnetic force drag properties to achieve the electrical conduction, electrical charge transfer and magnetising properties of the proposed contraceptive. Additionally the size and mechanical consistency of electrically conducting material and magnetic material are so selected that the mechanical characteristic impedance to the passage of ultrasound becomes significantly different from that of body tissue and hence the presence of the contraceptive within the body and its location can be determined by ultrasonography. Furthermore, the quantum of the presently

disclosed contraceptive within the reproductive tract can be determined non-invasively by magnetic field estimations as well as by X-ray imaging, CAT scan, MRI scan and scanning electrical impedance plethysmography.

This is an additional embodiment of the present invention that in order to restore the fertility, that is to remove the contraceptive from the reproductive tract, as and when desired by the subject, the contraceptive is heated by virtue of its electrical properties by electromagnetic induction with fields from outside the body. The heating changes the basic polymer characteristics thereby lowering its contraceptive action to obtain restoration of fertility as and when desired. Further embodiment of this invention includes lowering of viscosity of the contraceptive on induction heating which further facilitates the removal of the preparation from the body by an externally imposed magnetic field, preferably travelling magnetic field so as to restore reproductive functions as and when desired.

Still further embodiment of this invention includes that the swelling and anchoring properties of the presently disclosed contraceptive without adhesion gives long term retention for the contraception with a one time administration. The contraceptive of the presently disclosed invention may also be administered after removal if the person after a period of fertility restoration desires to have contraceptive status.

Yet another embodiment of this invention includes that the contraceptive preparation when placed in the vas deferens or the fallopian tube brings about changes in the sperm and/or ovum to result in contraceptive action. The change is effected by electrical charge properties of the contraceptive polymer; and the charge transfer, and sperm membrane and ovum cover molecule exchange capabilities of the electrically conducting material.

The removal of the contraceptive from the vas deferens or the fallopian tube, in accordance to the preferred embodiment of the present invention is possible by using the magnetic properties of the contraceptive preparation to propel the contraceptive for voiding and restoration of fertility by external magnetic field or alternately is possible by flushing by another injection of the pure solvent. However, reflushing of pure solvent is not intended to restrict the scope of the present invention.

The present invention therefore overcomes the disadvantages and limitations of the class of known contraceptives, which are used in the vas deferens and fallopian tube.

0.5mm. In accordance to this invention the microsize and macrosize particles of electrically conducting material are taken approximately in equal amounts by weight, and the microsize particles of magnetic material are taken in lower amount as compared to the macrosize particles of magnetic material. Further, in accordance with the present invention the quantum of electrically conducting material and magnetic material each varies between 3 to 20% by weight of the contraceptive polymer, particularly the electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of contraceptive polymer and magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of the contraceptive polymer.

In accordance to this invention the styrene maleic anhydride copolymer is prepared by the process known in the art or as disclosed in the *US Patent no. 5,488,075 and Indian Patent no. 183196* of the present inventor. The styrene maleic acid copolymer is prepared from styrene maleic anhydride copolymer either by the process known in the art or by the process disclosed herein after. For preparation of styrene maleic acid copolymer about 0.5gms of styrene maleic anhydride copolymer is taken in a round or flat bottom flask. About 50ml of about 0.5N NaOH is added to this amount of styrene maleic anhydride copolymer. The solution is left for refluxing for about 8 hrs. The refluxed material is allowed to cool down to ambient temperature followed by neutralisation with about 0.5N HCl till white precipitates of styrene maleic acid copolymer are formed. The precipitates of styrene maleic acid copolymer are separated and washed with distilled water and dried in vacuum. It is assured that styrene maleic anhydride copolymer and styrene maleic acid copolymer are free from their respective monomers.

In accordance to this invention, the presently disclosed contraceptive is prepared by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in the solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of the copolymers, the electrically conducting material and the magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C. The magnetic material is preferably the coated magnetic material to avoid aggregation of the magnetic particles. In accordance to preferred embodiment of this invention the copolymers, and the electrically conducting material and magnetic material are first mixed and then dissolved in the solvent.

acid copolymer, 5% of electrically conducting material and 10% of magnetic material and dissolving this mixed composition in about 99% pure dimethyl sulphoxide in the ratio in a manner that for every 100mg of the contraceptive polymer, that is for every 100mg of mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer about 200µl of dimethyl sulphoxide is added. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting and coated magnetic materials in the solvent is kept in nitrogen atmosphere and shaken for about 47 hrs by maintaining the temperature at about 35^0C. The resulting viscous contraceptive preparation is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

In accordance to another experiment of the present invention, 80mg of styrene maleic anhydride copolymer, 20mg of styrene maleic acid copolymer, 5mg of 99.9% pure copper particles consisting of microsize and macrosize particles and 10mg of coated iron particles consisting of microsize and macrosize particles are mixed with 200µl of about 99% pure dimethyl sulphoxide. The particle sizes of copper and iron particles are maintained within the limits described herein above. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, copper particles and coated iron particles in dimethyl sulphoxide is kept in nitrogen atmosphere and shaken for about 48 hrs by maintaining the temperature at 35^0C. The resulting viscous contraceptive preparation is ready for injection to the desired male or female and is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

The contraceptive of the present invention can be injected in male or female by any known means. However, specially designed process is described herein after merely for understanding and not to limit the scope of this invention. This described process is to take care of the specially embodied properties, particularly the charge transfer, electrical and magnetic properties of the presently disclosed contraceptive. In accordance to the preferred embodiment of the present invention the contraceptive preparation is taken in 250µl syringe, which is provided with about 23gauge needle.

In the male a puncture is made in the middle of the anterior surface of the scrotum, through which a small segment of vas deferens of the left side is delivered without injuring the vas deferens. This procedure is referred as 'no scalpel' procedure. Applying compression with the fingers onto the proximal portion of the vas deferens, that is towards

Claims

1. An improved injectable reversible contraceptive comprising a contraceptive polymer, a solvent medium, an electrically conducting material and magnetic material, characterised in that said contraceptive polymer is preferably from the hydrogel class of polymers, more preferably mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and said solvent medium is preferably dimethyl sulphoxide solvent, and said electrically conducting material and said magnetic material are essentially taken in particle forms of microsize and macrosize.

2. A contraceptive as claimed in claim 1, wherein styrene maleic acid copolymer and styrene maleic anhydride copolymer are taken in the ratio varying between 1.5:8.5 to 3:7, preferably 2:8 with respect to each other.

3. A contraceptive as claimed in claim 1, wherein said electrically conducting material is preferably copper in its pure form consisting of microsize particle and macrosize particle.

4. A contraceptive as claimed in claim 1, wherein said magnetic material is iron in pure form or in the form of oxide or a combination with copper or with a biologically accepted material like sulphur, more preferably magnetic material is iron in its pure form consisting of microsize particle and macrosize particle.

5. A contraceptive as claimed in claim 1, wherein said electrically conducting material and said magnetic material each varies between 3 to 20% by weight of said contraceptive polymer.

6. A contraceptive as claimed in claims 1 and 5, wherein said electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of said contraceptive polymer.

7. A contraceptive as claimed in claims 1 and 5, wherein said magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of said contraceptive polymer.

8. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of said electrically conducting material is about 0.005 to 20μ, preferably about 0.5 to 15μ and of said macrosize particles of said electrically conducting material is about 150μ to 0.2mm.

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 μl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claims 1 and 13, wherein said magnetic material is preferably coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body.

16. A contraceptive as claimed in claim 1, characterised in that the viscosity of the contraceptive is lowered on induction heating by an externally imposed electro-magnetic field.

17. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

18. A contraceptive as claimed in claim 1, characterised in that the contraceptive is controlled *insitu* by the application of a drag force or a propelling force by means of an external magnetic field.

19. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

20. A contraceptive as claimed in claim 1, characterised in that the flow of the contraceptive after injection is controlled by external means.

21. A contraceptive as claimed in claims 1 and 20, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

22. An improved injectable reversible contraceptive as claimed in claims 1 to 21 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 20 to 28 and substantially described herein above.

AMENDED CLAIMS
[received by the International Bureau on 25 August 2000 (25.08.00);
original claims 15 - 22 replaced by amended claims 15 - 20,
remaining claims unchanged (2 pages)]

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 μl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claims 1 and 13, wherein said magnetic material is preferably coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

16. A contraceptive as claimed in claims 1 or 15, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body, which in-turn causes lowering in viscosity of said contraceptive to effect the reversal thereof.

17. A contraceptive as claimed in claim 1, characterised in that the *in-situ* flow of the contraceptive after injection is controlled by external means, preferably by the application of a drag force or a propelling force by means of an external magnetic field.

18. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

19. A contraceptive as claimed in claims 1 or 18, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

20. An improved injectable reversible contraceptive as claimed in claims 1 to 19 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35°C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 20 to 28 and substantially described herein above.

STATEMENT UNDER ARTICLE 19 (1)

Originally **International / PCT Patent Application [No. PCT/IN 00/00023]** had 29 claims and now, after amendments by way of merging some claims, there are 27 claims. Original claims 1 to 14 and claims 23 to 29 are unchanged. Original claim 17 and 19 are also unchanged but amendments have necessitated their renumbering as claim 15 and 18 respectively. Original claims 15 and 16 are merged and are replaced by amended claim 16. Original claims 18 and 20 are also merged and are replaced by amended claim 17. Original claims 21 and 22 are replaced by amended claims 19 and 20 respectively. No new claim has been added.

The amended claims will not have any impact on the description as the amended claims do not go beyond the scope of the originally filed patent application.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Assistant Commissioner for Patents
United States Patent and Trademark Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 17 October 2000 (17.10.00)	
International application No. PCT/IN00/00023	**Applicant's or agent's file reference** IN/PA267/SKG
International filing date (day/month/year) 16 March 2000 (16.03.00)	**Priority date** (day/month/year) 17 March 1999 (17.03.99)
Applicant GUHA, Sujoy, Kumar	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

11 August 2000 (11.08.00)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer Olivia TEFY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* **IN/PA267/SKG**

Box No. I TITLE OF INVENTION

AN IMPROVED REVERSIBLE CONTRACEPTIVE FOR MALE AND FEMALE

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

GUHA, Sujoy Kumar
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Indian Institute of Technology Delhi (IITD)
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☒ This person is also inventor.

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91 11 659 1037 (Office)

Facsimile No. 91 11 658 1823 (Office)

Teleprinter No.

State *(that is, country)* of nationality: **IN**

State *(that is, country)* of residence: **IN**

This person is applicant for the purposes of: ☒ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

This person is:
☐ applicant only
☐ applicant and inventor
☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality:

State *(that is, country)* of residence:

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

MEHTA, Ramesh Kumar
Patent Attorney (Regn No. IN/PA-267)
Executive Consultant, Foundation for Innovation and Technology Transfer (FITT), Indian Institute of Technology Delhi (IITD), Hauz Khas, New Delhi-110016, INDIA

Telephone No. 91 11 685 7762(Office)
91116189141; 91116160423(Home)

Facsimile No. 91 11 685 1169(Office)
Telefax 91 11 618 9141 (Home)

Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

☒ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☒ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☒ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

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☒ **AU** Australia .....
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☒ **VN** Viet Nam .....
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Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

☐ .....
☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 17th March, 1999 (17.03.99)	415/DEL/99	IN		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): 1

* *Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*
ISA / EP

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*
Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request	:	3
description (excluding sequence listing part)	:	19
claims	:	3
abstract	:	1
drawings	:	
sequence listing part of description	:	
Total number of sheets	:	26

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☒ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify)*: PCT Request for reduction in EPO Fee

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Ramesh Cr Mehta.

(RAMESH KUMAR MEHTA)

[IN/PA - 267]

For receiving Office use only

1. Date of actual receipt of the purported international application:
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA /
6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

PCT

FEE CALCULATION SHEET

Annex to the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference: IN/PA267/SKG

Applicant: GUHA, Sujoy Kumar

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . INR 1,500=00 [T]

2. SEARCH FEE . . . . . USD 247=50 [S]

International search to be carried out by EP

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 26 sheets.

first 30 sheets . . . . . USD 427=00 [b1]

____ (remaining sheets) x ____ (additional amount) = — [b2]

Add amounts entered at b1 and b2 and enter total at B . . . . USD 427=00 [B]

Designation Fees

The international application contains All designations.

8 (number of designation fees payable *(maximum 8)*) x 92 (amount of designation fee) = USD 736=00 [D]

Add amounts entered at B and D and enter total at I . . . . . USD 290=75 [I]

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* . . . . . INR 1,000=00 [P]

5. TOTAL FEES PAYABLE . . . . . INR 2,500=00 USD 538=25 TOTAL

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☐ authorization to charge deposit account (see below)
☐ cheque
☐ postal money order
☒ bank draft
☐ cash
☐ revenue stamps
☐ coupons
☐ other *(specify)*:

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/

☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☐ *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

☐ is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.

Deposit Account No. | Date *(day/month/year)* | Signature

See Notes to the fee calculation sheet

IPEA/EP

PCT

DEMAND

Under Article 31 of the Patent Cooperation Treaty:
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated.)

For International Preliminary Examining Authority use only

Identification of IPEA	Date of receipt of DEMAND

Box No.I. IDENTIFICATION OF THE INTERNATIONAL APPLICATION		Applicant's or agent's file reference IN/PA267/SKG
International application No. PCT/IN 00/00023	International filing date (*day/month/Year*) 16 March, 2000 (16.03.00)	(Earliest) Priority date (*day/month/Year*) 17 March, 1999 (17.03.99)

Title of Invention: AN IMPROVED REVERSIBLE CONTRACEPTIVE FOR MALE AND FEMALE

Box No. II APPLICANT(S)

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country).*	Telephone No. 91-11-685 4211 (Home) 91-11-659 1037 (Office)
GUHA, Sujoy, Kumar Professor of Biomedical Engineering Centre for Biomedical Engineering (CBME) Indian Institute of Technology Delhi (IITD) Hauz Khas, New Delhi – 110016, INDIA	Facsimile No. 91-11-658 1823 (Office) Teleprinter No.
State (that is, country) nationality: IN	State (that is, country) of residence: IN

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country)*	
State (that is, country) of nationality:	State (that is, country) of residence:

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country)*	
State (that is, country) of nationality:	State (that is, country) of residence:

☐ Further applicants are indicated on a continuation sheet.

The following person is [redacted]

and ☐ has been appointed earlier and represents the applicant(s) also for international preliminary examination.

☒ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.

☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country).*	Telephone No.
MEHTA, Ramesh, Kumar Patent Attorney (Registration No. IN/PA-267) Remfry & Sagar, Attorneys-at-Law, Remfry House 8, Nangal Raya Business Centre New Delhi – 110046, INDIA	91-11-559 8072 (Office) Facsimile No. 91-11-559 8013 (Office) 91-11-559 4437 (Office) Teleprinter No.

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION

Statement concerning amendments:*

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filed

the description ☒ as originally filed

☐ as amended under Article 34

the claims ☐ as originally filed

☒ as amended under Article 19 (together with any accompanying statement)

☐ as amended under Article 34

the drawings ☐ as originally filed

☐ as amended under Article 34

☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.

2. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH

☒ which is the language in which the international application was filed.

☐ which is the language of a translation furnished for the purposes of international search.

☒ which is the language of publication of the international application.

☐ which is the language of the translation (to be) furnished for the purpose of international preliminary examination.

Box No.V ELECTION OF STATES

The applicant hereby elects ALL eligible States (*that is, all States which have been designated and which are bound by Chapter II of the PCT*)

excluding the following States which the applicant wishes not to elect:

examination.					
1. translation of international application	:		sheets	☐	☐
2. amendments under Article 34	:		sheets	☐	☐
3. copy (or, where required, translation) of amendments under Article 19	:	Four	sheets	☐	☐
				☐	☐
4. copy (or, where required, translation) of statement under Article 19	:	One	sheet	☐	☐
5. letter	:	Two	sheets	☐	☐
6. other (specify) Copy of Letter to IB u/A-19	:	Two	sheets		
EPO Form 1223/A	:	One	sheet		

The demand is also accompanied by the item(s) marked below:

1. ☒ Fee calculation sheet
2. ☒ Separate signed power of attorney
3. ☐ copy of general power of attorney;

reference number, if any:

4. ☐ statement explaining lack of signature
5. ☐ nucleotide and or amino acid sequence listing in computer readable form
6. ☒ other (*specify*): Copy of Letter to IB u/A-19 EPO Form 1223/A

Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

Damesh CrMehl

(Dr. Ramesh Kumar MEHTA)
Patent Agent for THE APPLICANT
(Registration No. IN/PA-267)

Place : New Delhi, INDIA **Date : 18 September, 2000 (18.09.00)**

For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:
2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):
3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5 below, does not apply. ☐ The applicant has been informed accordingly.
4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.
5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

For International Bureau use only

Demand received from IPEA on:

See Notes to the demand form

FEE CALCULATION SHEET

Annex to the Demand for international preliminary examination

For International Preliminary Examining Authority use only

International Application No. PCT/IN 00/00023	
Applicant's or agent's File reference IN/PA267/SKG	Date stamp of the IPEA

Applicant. GUHA, Sujoy, Kumar

Calculation of prescribed fees

1. Preliminary examination fee..... CHF 620.00 P

2. Handling fee *(Applicants from certain States are entitled to a reduction of 75% of the handling fee. Where the applicant is (or all applicants are) so entitled, the amount to be entered at H is 25% of the handling fee.)* ..... CHF 58.25 H

3. Total of prescribed fees
Add the amounts entered at P and H
And enter total in the TOTAL box..... CHF 678.25 TOTAL

Mode of Payment

- ☐ authorization to charge deposit account with the IPEA (see below)
- ☐ cash
- ☐ cheque
- ☐ revenue stamps
- ☐ postal money order
- ☐ coupons
- ☒ bank draft
- ☐ other *(specify)*:

Deposit Account Authorization (this mode of payment may not be available at all IPEAs)

The IPEA/ _____ ☐ is hereby authorized to charge the total fees indicated above to my deposit account.

☐ (this check-box may be marked only if the conditions for deposit accounts of the IPEA so permit) is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account.

Deposit Account Number _____ Date (*day/month/year*) _____ Signature _____

See Notes to the fee calculation sheet

examination in favour of nationals of certain states which fulfil the requirements for the corresponding reduction in PCT fees payable to the International Bureau of WIPO

(Decision of the Administrative Council of the European Patent Organisation of 14 June 1996, OJ EPO 1996, 396)

To Addressee a)

The Controller of Patents
The Patent Office
Govt. of India
Patent Office Branch, Delhi
3rd Floor, M. M. Building
Karol Bagh, New Delhi - 110 005
India

a) The addressee is the receiving Office (see notes point 4) or the EPO (see notes point 5)

Applicant's or agent's file reference (indicated by applicant if desired)

IN/PA267/SKG

I. Identification of the international application (must be consistent with PCT request/if known)

International application No. b)	International filing date b)	Priority date
		17th March, 1999 (17.03.99)

b) These boxes are not to be completed if, at the time the request is made, the applicant has not yet been notified of the international filing number or date

Title of invention

AN IMPROVED REVERSIBLE CONTRACEPTIVE FOR MALE AND FEMALE

II. Request

The applicant(s) identified below (Box IV) herewith request(s) a 75% reduction in the

☒ EPO international search fee

☒ EPO preliminary examination fee

in respect of the above international application, in accordance with the Decision of the Administrative Council of the European Patent Organisation of 14 June 1996.

III. Declaration

Pre-crossed because condition sine qua non (see notes point 2) The applicant(s) confirm(s) this declaration by signing Box V, to be checked by receiving Office

☒ The applicant(s) identified below (Box IV) affirm(s) that the information regarding nationality, residence and/or principal place of business is true (see notes point 2,5)
Furthermore the applicant(s) affirm(s) that natural or legal persons who are not nationals of or who do not have their residence or principal place of business in states which fulfil the requirements for the corresponding reduction in PCT fees payable to the International Bureau of WIPO have neither a direct nor an indirect holding or interest (cf. PCT Gazette, Section IV)

GUHA, Sujoy Kumar

Professor of Biomedical Engineering, Centre for Biomedical Engineering (CBME)

Indian Institute of Technology Delhi (IITD), Hauz Khas, New Delhi-110016, INDIA

State (ie country) of nationality	State (ie country) of residence or principal place of business	
IN	IN	
Telephone (if any) 91 11 659 1949 (Home) 91 11 659 1037 (Office)	Fax (if any) 91 11 686 2037 (Office)	Telex (if any)

V. Signature of applicant(s) *(Cf. also Notes to Box No. IX of PCT Request Form PCT/RO/101)*

Please type the name of each person signing the request below his signature. The request may be signed by an agent or the common representative (Rules 2 1, 90 PCT)

(RAMESH KUMAR MEHTA)
Patent Agent for The Applicant (IN/PA-267)

Place NEW DELHI, INDIA Date 16th March, 2000 (16.03.00)

The following boxes are for the use of the receiving Office and European Patent Office respectively

The _____ *(specify)* acting as receiving Office ☐ grants the request for a reduction in the international search fee. ☐ does not grant the request for the reasons given on the attached supplementary sheet ☐ A copy of the fee reduction request indicating the above decision has been sent to the EPO branch at The Hague.	Authorised official: Date:
The European Patent Office acting as International Preliminary Examining Authority ☐ grants the request for a reduction in the international preliminary examination fee. ☐ does not grant the request for the reasons given on the attached supplementary sheet	Authorised official: Date:

EPO Form 1223/A 08.96

Attorneys-at-Law
Remfry House
8, Nangal Raya Business Centre, New Delhi - 110 046
Tel: 91-11- 559 8072 (4 Lines) Fax: 91-11-559 4437, 559 8013 E-Mail: remfry-sagar@remfry.com http:// www.remfry.com

RKM/IP : PCT/IN 00/00023 September 18, 2000

Copy by Fax No. : 31-70-340-3016

International Preliminary Examination Authority (IPEA)
European Patent Office
The Hague
Patentlaan 2
Postbus 5818, 2280 HV Rijswijk
NETHERLANDS

Dear Sirs,

Reference : **International Preliminary Examination of**
PCT/International Patent Application No. PCT/IN 00/00023
International Filing Date : March 16, 2000 [16/03/2000]
Priority Date : March 17, 1999 [17/03/1999]
Agent's File Reference No. IN/PA267/SKG
Applicant : GUHA, Sujoy, Kumar
In Chapter II – International Phase

The International Search Report (ISR) in respect of the International /PCT Patent application no. PCT/IN 00/00023 has been issued and was mailed to us on 10 August 2000 (10.08.00) by International Searching Authority (ISA) – European Patent Office (EP).

The Applicant has amended the claims under Article 19 of the provisions of PCT. The amendments to the claims under Article 19 have been received by International Bureau (IB), Geneva on 25 August 2000 (25.08.00). The International application will be published on 21 September 2000 (21.09.00). The Applicant has opted for Chapter II – International Phase for International Preliminary Examination through your Authority.

This letter is to request you to conduct the International Preliminary Examination of the above noted International/PCT Patent Application No. PCT/IN 00/00023.

The following documents accompany this request :-

a) PCT Demand Form – PCT/IPEA/401
b) PCT Fee calculation sheet, Annex to the Demand for International preliminary examination
c) Copy of letter addressed to IB, Geneva for amendments of the claims under Article 19 of the provisions of PCT with "Amendments under Article 19".
d) "Statement under Article 19(1)" of the provisions of PCT.

e) The replaced sheets 21 and 22, with claims as originally filed.
f) The replacement sheets 21 and 22 with amended claims.
g) Request for reduction in the EPO fees for the international search and preliminary examination on EPO Form 1223/A, as submitted to the Receiving Office, The Patent Office, Government of India on 16 March, 2000 (16.03.00) along with PCT application.
h) The fresh Power of Attorney.

The Applicant intends to reserve the right to amend the description and/or claims, if required, under Article 34 of the provisions of PCT.

Please confirm the calculation of the fee as per enclosed Fee Calculation Sheet and kindly inform that in whose favour the bank draft is to be drawn for payment of the International Examination Fee and Handling Fee.

Thanking you,

Yours faithfully,

(Dr. Ramesh Kumar MEHTA)
Registered Indian Patent Agent
(Registration No. IN/PA-267)
PATENT AGENTS FOR THE APPLICANT
of REMFRY & SAGAR

Enclosures : **As stated above**
PCT Demand Form – PCT/IPEA/401 – three sheets
PCT Fee calculation sheet – one sheet
Letter to IB – two sheets
Statement Under Article 19(1) – one sheet
Replaced Sheets nos. 21 and 22, as originally filed – two sheets
Replacement Sheets nos. 21 and 22, as amended – two sheets
EPO Form 1223/A – one sheet
Power of Attorney – one page
Total fifteen sheets including two sheets of this Request letter

To accompany the copy by post

Copy to **European Patent Office**
Erhardtstr. 27
D-80298
MUNICH, GERMANY
FAX NO. 49-89-2399-4465
TELEPHONE NO. 49-89-2399-0

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
IN/PA267/SKG		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IN00/00023	16/03/2000	17/03/1999
International Patent Classification (IPC) or national classification and IPC A61K9/10		
Applicant GUHA, Sujoy, Kumar		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 9 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11/08/2000	18.06.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hedegaard, A Telephone No. +49 89 2399 8644

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IN00/00023

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-7,10,13,14,16, 18,19	as originally filed	
8,9,11,12,15,17	with telefax of	26/02/2001

Claims, No.:

1,2,4-20,23-29	with telefax of	26/02/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 20,29.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 20,29 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-2, 4-19, 23-28
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-2, 4-19, 23-28

	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-2, 4-19, 23-28
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Section III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No meaningful opinion can be given for the subject-matter of claims 20 and 29 since the vague wording "substantially described herein above" renders the scope of the claims unclear (Art. 6 PCT).

Re Section V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

   D1: Chemical abstracts, vol. 109, no. 25 (1988-12-19) abstract no. 223418

2. The subject-matter of claims 1-2 and 4-19 is novel (Art. 33(2) PCT) since an injectable reversible contraceptive comprising (i) a contraceptive polymer from the hydrogel class of polymers, (ii) dimethyl sulphoxide solvent, (iii) an electrically conducting material which is copper in its pure form and (iv) a magnetic material which is iron in its pure form has not been disclosed in the available prior art documents.

3. The subject-matter of claims 23-28 is novel (Art. 33(2) PCT) since a process according to independent claim 23 comprising the steps of dissolving styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in a solvent medium, followed by keeping the complex solution of said copolymer in an inert environment and shaking for 45-50 hrs by maintaining the temperature at 35°C has not been disclosed in any of the available prior art documents.

4. D1 (closest prior art) discloses image forming contraceptives comprising nylon, ethanol, phenol, Cu-Zn alloys and glycerol. The subject-matter of present claim 1 differs from that of D1 in specifying (i) a certain polymer, namely from the hydrogel class, (ii) a certain solvent, namely dimethyl sulphoxide, (iii) a certain electrically conducting material, namely copper in its pure form and (iv) a certain magnetic material, namely iron in its pure form.

It could not be foreseen from D1, alone or in combination with another document, that contraceptives according to the present claim 1 would not only act as a blocking agent but brings about changes in the sperms and/or ovum. Furthermore, there is no hint in D1 to propel the contraceptives by means of an external magnetic field as is this case with the present contraceptives comprising a certain magnetic material.

Therefore, the subject-matter of claims 1-2 and 4-19 is considered to involve an inventive step (Art. 33(3) PCT).

The same applies mutatis mutandis to the process claims 23-28 (see however below under section VIII, item 1).

Re Section VIII

Certain observations on the international application

1. In order to keep the linking concept of the invention claim 23 should have a reference to claim 1 and the term "preferably" be deleted (Rule 13.1 PCT).

2. The words "about" and "approximately" detract from the general clarity of claims 6-10, 12 and 23 (Art. 6 PCT).

3. The claims should be renumbered due to the deleted claims 3 and 21-22 (Art. 6 PCT).

4. A discrepancy exists between independent claim 1 (iron in its pure form) and dependent claim 4 (iron in the form of oxide or a combination with a biologically accepted material); Art. 6 PCT.

retrograde actum on the ovary in the female, which reduces the chance of actual fertility restoration even when by surgery the device is removed or replaced by another such device for restoring fertility. Still another disadvantage of such known devices is that the insertion into the urethra of some of such devices either permanently, till desired by the patient or temporarily, for each act of intercourse, is painful and likely to produce erosion and infection. Yet another disadvantage of such known devices is that the use of some of such devices requires attention of the user prior and after such intercourse. Further disadvantage associated with such known devices is that the large size of some of such devices leads to rupture of the vas deferens in many cases. Still further disadvantage associated with such known devices is that the use of some of such devices totally destroys a segment of the vas deferens and/or fallopian tube, hence reversal would require special microsurgery to rejoin the vas deferens and/or fallopian tube. Yet further disadvantage associated with such known devices is that the removal of some of such devices becomes difficult and calls for a complicated procedure on account of fibrosis with low success rate. Yet another class of occlusion methods to achieve contraception or sterilization includes formation of a chemical preparation based plug in the vas deferens and/or fallopian tube, such as formation of polyurethane plug (*UK Patent no. GB2223025*) or nylon plug (CN 85108504A) or neem oil plug (*US Patent no. 5,501,855*) or styrene maleic anhydride copolymer plug (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The polyurethane plug is formed by reacting pre-polymer of polyurethane with a chain-enlargement agent with amino-group under normal atmospheric temperature or above it in the presence of an organic solvent and organic acid catalyst, which is solidified in the ductus deferens (*UK Patent no. GB2223025*). The reversibility is achieved by removal of the plug. The nylon plug is formed by reacting nylon, EtOH, phenol, Cu-Zn alloys and glycerol which also results in blockage of oviduct or vas deference (CN85108504). The neem oil plug is formed by intra-vas administration of neem oil to male rats, which resulted in blockage of spermatogenesis without affecting the testosterone production (*US Patent no. 5,501,855*). The reversibility has not been achieved. The styrene maleic anhydride copolymer plug is formed by step irradiation of styrene maleic anhydride at a dose of 0.2 to 0.24 megarad for its every 40 gms followed by dissolution in pure dimethyl sulphoxide and thereafter injected into the lumen of the vas deferens (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The reversibility is achieved by flushing of the styrene maleic anhydride copolymer plug by injecting extra dose of pure dimethyl

sulphoxide. The polyurethane and nylon plugs suffer from similar disadvantages as that of the contraceptive devices for use by male or by male and female, as described herein above. The neem oil plug preparation has limitation that, it does not polymerise rapidly after injection and hence travels retrograde into the testes. Further, it causes damages to the testes and testicular size reduces. Still further disadvantage of neem oil plug is that the lymph nodes are affected. Yet another limitation of the neem oil plug is that the restoration of fertility is not possible.

The styrene maleic anhydride copolymer plug, herein after referred to as SMA plug, which is undergoing multicentric Phase-III Clinical Trials in India and has been developed by the inventor of the presently disclosed invention, has been observed to have certain limitations, such as, it cannot be detected and/or suitably quantified externally by means of X-ray, CAT scanning, magnetic resonance imaging (MRI) or magnetic field due to the non-radio-opaque nature of the contraceptive drug. Another limitation of SMA plug is that, its spread or distribution in the reproductive tract after injection cannot be controlled. Further limitation of SMA plug is that, for its removal to restore the fertility, another injection of extra dose of dimethyl sulphoxide is required to be given to the patient, hence it cannot be removed from the body conveniently by non-invasive and external means except by using the reversal device disclosed in the *pending Indian Patent application no. 928/DEL/97*, developed by inventor of the present invention. However, the removal of the contraceptive even by this device is not 100% successful due to the difficulty in removal of the contraceptive from the part of vas deferens leading to the prostate region.

The limitations of SMA plug, as described herein above, have also been observed in other similar contraceptive preparations, such as polyurethane plug, neem oil etc., which are intended to be used by male or female or male and female for blockage of the vas deferens and/or fallopian tube by way of formation of plug or for affecting the nature of sperm and/or ovum for achieving the contraception or sterilization, as the basic compound of the such known contraceptive preparations being non-radio-opaque and non-magnetic in character. The MRI also fails to detect the contraceptive mainly due to its poor contrast with the soft tissue. The ultrasound is also incapable of detecting the contraceptive, due to low percentage of the basic compound and inadequate difference of the characteristic impedance from the body tissue. To overcome this disadvantage, if the net percentage of the basic compound is increased, it will have the disadvantages

This is further an object of this invention to disclose a contraceptive which necessarily does not require any surgery or flushing of any solvent for its removal from the reproductive duct to restore the fertility and can be removed from the body by non-invasive and external means. This is still an object of this invention to disclose a contraceptive, which is required to be injected only once for achieving contraception.

This is yet an object of this invention to disclose a contraceptive which can be reversed by external non-invasive means and necessarily does not require additional injection of an extra dose of the pure solvent, thus avoid the second injection.

This is still further an object of this invention to disclose a contraceptive which not only acts as a blocking agent but also brings about changes in the sperm and/or ovum to result in the contraceptive action, hence overcome the disadvantages associated with the contraceptives capable of acting as blocking agent alone.

Brief Description and Preferred Embodiments of the Invention :-

Accordingly this invention provides a complete disclosure of an injectable reversible contraceptive and the method of preparation and use thereof, having above stated characteristics and consisting of contraceptive polymer, a solvent medium, an electrically conducting material and a magnetic material, characterised in that the contraceptive polymer is from the hydrogel class of polymers, particularly a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and the solvent medium is dimethyl sulphoxide solvent, and the electrically conducting material is copper in its pure form essentially consisting of microsize particles and macrosize particles, and the magnetic material is iron in its pure form essentially consisting of microsize particles and macrosize particles, particularly it discloses a contraceptive consisting of contraceptive polymer having electrical charge and pH lowering properties, a solvent medium having complexing properties, an electrically conducting material having charge transfer, sperm membrane and ovum covering molecule exchange, and inductive heating properties and magnetic material having magnetising and magnetic force drag properties to achieve the electrical conduction, electrical charge transfer and magnetising properties of the proposed contraceptive. Additionally the size and mechanical consistency of electrically conducting material and magnetic material are so selected that the mechanical characteristic impedance to the passage of ultrasound becomes significantly different from that of body tissue and hence the presence of the contraceptive within the body and its location can be determined by ultrasonography. Furthermore, the quantum of the presently

disclosed contraceptive within the reproductive tract can be determined non-invasively by magnetic field estimations as well as by X-ray imaging, CAT scan, MRI scan and scanning electrical impedance plethysmography.

This is an additional embodiment of the present invention that in order to restore the fertility, that is to remove the contraceptive from the reproductive tract, as and when desired by the subject, the contraceptive is heated by virtue of its electrical properties by electromagnetic induction with fields from outside the body. The heating changes the basic polymer characteristics thereby lowering its contraceptive action to obtain restoration of fertility as and when desired. Further embodiment of this invention includes lowering of viscosity of the contraceptive on induction heating which further facilitates the removal of the preparation from the body by an externally imposed magnetic field, preferably travelling magnetic field so as to restore reproductive functions as and when desired.

Still further embodiment of this invention includes that the swelling and anchoring properties of the presently disclosed contraceptive without adhesion gives long term retention for the contraception with a one time administration. The contraceptive of the presently disclosed invention may also be administered after removal if the person after a period of fertility restoration desires to have contraceptive status.

Yet another embodiment of this invention includes that the contraceptive preparation when placed in the vas deferens or the fallopian tube brings about changes in the sperm and/or ovum to result in contraceptive action. The change is effected by electrical charge properties of the contraceptive polymer; and the charge transfer, and sperm membrane and ovum cover molecule exchange capabilities of the electrically conducting material.

The removal of the contraceptive from the vas deferens or the fallopian tube, in accordance to the preferred embodiment of the present invention is possible by using the magnetic properties of the contraceptive preparation to propel the contraceptive for voiding and restoration of fertility by external magnetic field or alternately is possible by flushing by another injection of the pure solvent.

The present invention therefore overcomes the disadvantages and limitations of the class of known contraceptives, which are used in the vas deferens and fallopian tube.

0.5mm. In accordance to this invention the microsize and macrosize particles of electrically conducting material are taken approximately in equal amounts by weight, and the microsize particles of magnetic material are taken in lower amount as compared to the macrosize particles of magnetic material. Further, in accordance with the present invention the quantum of electrically conducting material and magnetic material each varies between 3 to 20% by weight of the contraceptive polymer, particularly the electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of contraceptive polymer and magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of the contraceptive polymer.

In accordance to this invention the styrene maleic anhydride copolymer is prepared by the process known in the art or as disclosed in the *US Patent no. 5,488,075 and Indian Patent no. 183196* of the present inventor. The styrene maleic acid copolymer is prepared from styrene maleic anhydride copolymer either by the process known in the art or by the process disclosed herein after. For preparation of styrene maleic acid copolymer about 0.5gms of styrene maleic anhydride copolymer is taken in a round or flat bottom flask. About 50ml of about 0.5N NaOH is added to this amount of styrene maleic anhydride copolymer. The solution is left for refluxing for about 8 hrs. The refluxed material is allowed to cool down to ambient temperature followed by neutralisation with about 0.5N HCl till white precipitates of styrene maleic acid copolymer are formed. The precipitates of styrene maleic acid copolymer are separated and washed with distilled water and dried in vacuum. It is assured that styrene maleic anhydride copolymer and styrene maleic acid copolymer are free from their respective monomers.

In accordance to this invention, the presently disclosed contraceptive is prepared by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in the solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of the copolymers, the electrically conducting material and the magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C. The magnetic material is coated magnetic material to avoid aggregation of the magnetic particles. In accordance to preferred embodiment of this invention the copolymers, and the electrically conducting material and magnetic material are first mixed and then dissolved in the solvent.

acid copolymer, 5% of electrically conducting material and 10% of magnetic material and dissolving this mixed composition in about 99% pure dimethyl sulphoxide in the ratio in a manner that for every 100mg of the contraceptive polymer, that is for every 100mg of mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer about 200µl of dimethyl sulphoxide is added. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting and coated magnetic materials in the solvent is kept in nitrogen atmosphere and shaken for about 47 hrs by maintaining the temperature at about 35°C. The resulting viscous contraceptive preparation is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

In accordance to another experiment of the present invention, 80mg of styrene maleic anhydride copolymer, 20mg of styrene maleic acid copolymer, 5mg of 99.9% pure copper particles consisting of microsize and macrosize particles and 10mg of coated iron particles consisting of microsize and macrosize particles are mixed with 200µl of about 99% pure dimethyl sulphoxide. The particle sizes of copper and iron particles are maintained within the limits described herein above. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, copper particles and coated iron particles in dimethyl sulphoxide is kept in nitrogen atmosphere and shaken for about 48 hrs by maintaining the temperature at 35°C. The resulting viscous contraceptive preparation is ready for injection to the desired male or female and is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

The contraceptive of the present invention can be injected in male or female by any known means. However, specially designed process is described herein after merely for understanding. This described process is to take care of the specially embodied properties, particularly the charge transfer, electrical and magnetic properties of the presently disclosed contraceptive. In accordance to the preferred embodiment of the present invention the contraceptive preparation is taken in 250µl syringe, which is provided with about 23gauge needle.

In the male a puncture is made in the middle of the anterior surface of the scrotum, through which a small segment of vas deferens of the left side is delivered without injuring the vas deferens. This procedure is referred as 'no scalpel' procedure. Applying compression with the fingers onto the proximal portion of the vas deferens, that is towards

Claims

1. An injectable reversible contraceptive comprising a contraceptive polymer, a solvent medium, an electrically conducting material and a magnetic material, characterised in that said contraceptive polymer is from the hydrogel class of polymers, particularly a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and said solvent medium is dimethyl sulphoxide solvent, and said electrically conducting material is copper in its pure form essentially consisting of microsize particles and macrosize particles, and said magnetic material is iron in its pure form essentially consisting of microsize particles and macrosize particles.

2. A contraceptive as claimed in claim 1, wherein styrene maleic acid copolymer and styrene maleic anhydride copolymer are taken in the ratio varying between 1.5:8.5 to 3:7, preferably 2:8 with respect to each other.

3. Deleted.

4. A contraceptive as claimed in claim 1, wherein said magnetic material is iron in the form of oxide or a combination with a biologically accepted material, like sulphur, essentially consisting of microsize particles and macrosize particles.

5. A contraceptive as claimed in claim 1, wherein said electrically conducting material and said magnetic material each varies between 3 to 20% by weight of said contraceptive polymer.

6. A contraceptive as claimed in claim 5, wherein said electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of said contraceptive polymer.

7. A contraceptive as claimed in claim 5, wherein said magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of said contraceptive polymer.

8. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of said electrically conducting material is about 0.005 to 20μ, preferably about 0.5 to 15μ and of said macrosize particles of said electrically conducting material is about 150μ to 0.2mm.

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 µl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claim 13, wherein said magnetic material is coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

16. A contraceptive as claimed in claims 1 or 15, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body, which in-turn causes lowering in viscosity of said contraceptive to effect the reversal thereof.

17. A contraceptive as claimed in claim 1, characterised in that the *in-situ* flow of the contraceptive after injection is controlled by external means, preferably by the application of a drag force or a propelling force by means of an external magnetic field.

18. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

19. A contraceptive as claimed in claims 1 or 18, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

20. An injectable reversible contraceptive as claimed in claims 1 to 19 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid

copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 23 to 28 and substantially described herein above.

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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Applicant
GUHA, Sujoy, Kumar

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

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(54) Title: AN IMPROVED REVERSIBLE CONTRACEPTIVE FOR MALE AND FEMALE

(57) Abstract

The present invention relates to an improved injectable reversible contraceptive for use by male and female comprising a contraceptive polymer, a solvent medium, an electrically conducting material and magnetic material, characterised in that the contraceptive polymer is a mixture of styrene maleic anhydride and styrene maleic acid copolymers, and the solvent medium is dimethyl sulphoxide solvent, and the electrically conducting material is copper particles and magnetic material is iron particles both consisting of microsize and macrosize particles. The contraceptive is prepared by mixing the weighed quantities of copolymers and electrically conducting and magnetic materials and dissolving in dimethyl sulphoxide followed by keeping this complex solution in an inert environment and shaking for about 45–50 hrs by maintaining the temperature at about 35 °C.

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An Improved Reversible Contraceptive for Male and Female

Technical Field of the Invention :-

The present invention relates to an improved reversible contraceptive for use by male and female, particularly it relates to an injectable reversible contraceptive consisting of contraceptive polymer, an electrically conducting material and magnetic material in a solvent medium, more particularly it relates to an injectable reversible contraceptive consisting of copolymers of styrene maleic anhydride and styrene maleic acid, and micro and macro size particles of magnetic material and electrically conducting material in pure dimethyl sulphoxide having improved contraceptive action as well as more controlled delivery method and reversal action to restore fertility and capable of imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography, and capable of better control and determination of quantum of distribution within the reproductive ducts by external magnetic field.

Background Art of the Invention :-

The progeny is formed by the union of the male sperms and the female ovum, a process known as fertilization. In the male the sperms travel from the testes via the epididymis along a tube known as vas deferens. In the female the ovum comes down the tube known as fallopian tube also as the oviduct and the sperms from the male travel up this same tube and fusion of the sperm and the ovum takes place in the fallopian tube. If by surgical means or placement of a contraceptive device or a preparation in the male vas deferens, the biological activity of the sperm is significantly altered then the sperms will not be able to effectively fuse with the ovum and produce a progeny. Similarly, if by the surgical means or placement of a contraceptive device or a preparation in the female fallopian tube a significant alteration in either the sperm or the ovum or both is caused, then the fusion of the sperm and the ovum is prevented and fertilization followed by progeny development does not take place. Various surgical means and contraceptive devices and preparations have been developed over last few decades to avoid fertilization followed by progeny development.

One of the known surgical means, which is commonly used and known as vasectomy consists of cutting and tying the vas deferens in males. Similar operation in the female is known as tubectomy, which involves cutting and tying of the fallopian tube in female. This surgical procedure results in prevention of flow of sperms through vas deferens in males and flow of ovum through fallopian tube in females in forward direction.

The major disadvantage of vasectomy is that it is surgical in nature and the reversal of the fertility is not effective. The rejoining or opening of vas deferens or of fallopian tube does not result in the desired fertility, because the level of generation of antibodies even after rejoining or opening of vas deferens remains high, which in turn continue to destroy the sperms. In the female rejoining or opening of the fallopian tube often produces inadequate transport of ovum.

Another class of known contraceptives in the art for the male includes repeated administration of androgens, such as testosterone enanthate. A regimen of weekly intra-muscular injection of 200 mg of testosterone enanthate was tried in men [*Lancet (1990) 338 (8721) : 955-959*]. The trials in animals resulted azoospermia or oligospermia in most of the animals [*Fertil. Steril. (1977) 28 : 1320-1328*], and trials in men resulted in azoospermia in about 55% of subjects with oligospermia observed in a further 40%. Other side effects included weight gain, greasiness of skin and lowering of high density serum lipoproteins, which are thought to be cardioprotective [*J.Clin.Endocrinol.Metab. (1991) 73 : 4-7*]. An attempt to find more effective androgens resulted in development of a drug 17a-beta-hydroxy-7-alpha-methyl-D-homo-19-norandrost-4, 16-diene-3-one and its 17a-beta hydroxy esters (*US Patent no. 4,788,218*). These were found to be active by subcutaneous injection, maintaining libido, however, consistent reduction in spermatogenesis could not be obtained. Further research led to development of long acting esters of testosterone, like testosterone buciclate with the general formula Tes-CO-R-R' (*US Patent no. 4,948,790*), which have shown high effectiveness in animals to suppress spermatogenesis. Although, these drugs held promise, results from various trials indicated that periodic administration of supra-physiological doses of androgens alone led to wide fluctuations in androgen levels and hence sustained release methods were advocated.

Still another class of known contraceptives in the art is combination of androgens with progestagens, which have shown certain advantages over the androgens alone *[Fertil. Steril. (1989) 52(6):1011-1018 and Fertil. Steril. (1993) 60(6):1062-1068*]. Even studies of this class of contraceptives indicated some problems, such as need for quite high doses of gestagen and adverse side effects on account of the oestrogenic activity of the gestagen. Yet another class of known contraceptives in the art is of gonadotrophin releasing hormone (GnRH) or luteinising hormone releasing hormone (LHRH) [*New Engl. J.Med. (1981) 305 : 663-667*], which due to accompanied decreased libido and potency suggested a need for addition of testosterone. Further, some of the agonists of LHRH are resistant to

biodegradation. Therefore, the LHRH agonist approach is no longer being pursued. Instead, LHRH antagonists, the another class of the known contraceptives appeared to be very promising. Quite a large number of these antagonists have been made available (*US Patent no. 5,171,835*) and [*J.Clin.Endocrinol.Metab. (1993) 77(2):427-432*]. Such antagonists suffer from the limitation of requirement of judicious balance between testosterone suppression and supplementation. It is unlikely that a fixed dose schedule effective in all men will ever be realised and hence their practical utility will probably be limited.

Further class of known contraceptives in the art was of anti-androgens, which were studied for their contraceptive action [*Contraception (1976) 14:403-407*]. Cyproterone acetate (CPA), which was administered orally and from subcutaneous implants, was thought at that time to inhibit supermatozoan maturation in the epididymis. However, on account of side effects, especially libido reduction, at the doses necessary to induce azoospermia or oligospermia, this compound and anti-androgens as such were virtually given up. Now combination of oral cyproterone acetate with testosterone like injectables are being assessed, but duration of effectiveness and efficacy in the people of all ethnic origin is not satisfactory.

Still further class of known contraceptives in the art was of follicle stimulating hormone (FSH) inhibiting proteins (*US Patent No. 5,015,729 and 5,037,805*). Although, these drugs have shown promising results during clinical trials, but the outcome is very species specific and effective long-term immunogenicity seems difficult. Hence, despite advances in the synthetic chemistry of human inhibin, the possible role in human fertility control is far from clear. None of the immunological drugs have undergone long-term trials.

Yet another class of known contraceptives in the art is of astringents like zinc and tannins (*US Patent No. 4,156,427*) and glycerol (*US Patent No. 4,720,507*). Such contraceptives are directly injected into testes, which often results in testicular atrophy and generally leads to permanent sterilization with no scope of reversal, even with surgical intervention. Practical drugs for reversible contraception on this basis are yet to be tried.

Still another known contraceptive in the art consists of un-complexed microsize particles of copper of size between 0 to 90μm alone taken in castor oil, which is injected into the epididymis in a 'blind approach' [*Int.J.Andrology (1985) 8:168-174*]. The major disadvantage of such use of un-complexed microsize particles of copper in castor oil is

that the contraceptive in part enters in the epididymal tubule and more so remain outside the tubule and therefore produces histological damage to the epididymis and there being no control on backtracking of the contraceptive preparation into the testes and hence the testicular tissue is adversely affected. By this means the contraception is achieved in majority of animals tested but not in all and further along with the contraceptive effect the adverse effects on account of tissue damage occurs. Furthermore, there is no scope of removal of the contraceptive preparation for restoration of fertility. Yet another known contraceptive in the art consists of exclusively un-complexed microsize particles of copper, which are neither injected in the vas deferens or epididymis nor in the fallopian tube but are inserted in the wall of the vas deferens by means of iontophoresis of copper [*Andrologia (1982) 14:481*]. This contraceptive has short lived contraceptive effect and the planned removal of the contraceptive from the wall of the vas deferens to restore fertility prior to self reversal time is not possible.

Still another class of known contraceptives is in the form of contraceptive device, which can be inserted in the vas deferens or the fallopian tube. The major disadvantage of the contraceptive devices is that generally these are non-reversible with some exceptions.

One class of known contraceptive devices in the art is of those using copper in its wire form only. Such contraceptive devices include contraceptive device consisting of copper in wire form only, which is inserted into lumen of the vas deferens [*Contraception (1994) 29:45-48*] or contraceptive device consisting of copper in wire form only, which is inserted into the lumen of the fallopian tube [*Indian J.Exp. Biol. (1976) 14:316-319*]. The major disadvantage of using such contraceptive devices consisting of copper in wire form only is that such form of copper is fairly stiff structure and generally causes injury to the vas deferens or the fallopian tube, as the case may be and may often cause puncture, which may result in irreversible damage to the vas deferens or the fallopian tube. Further disadvantage of using wire form of copper as contraceptive device in male or female is that such form of copper may subsequently cause fibrosis, which makes the removal of the wire form of copper device difficult with very low return of fertility.

Another class of contraceptive device known in the art, which uses copper or its alloy in its coil form only is of a contraceptive device consisting of the copper or its alloy only in the form of coil, which is given a shape to have larger surface area and is anchored within the fallopian tube by a lumen traversing region of the resilient structure which has a helical outer surface, together with a portion of the resilient structure which is biased to

form a bent secondary shape, the secondary shape having a larger cross-section than the fallopian tube. The resilient structure is restricted in a straight-configuration and trans-cervically inserted within the fallopian tube, where it is released [*Patent Application no. WO 99/15116, date of publication 10.08.99*]. Still another known contraceptive device consists of copper in its ring form disposed between the ribs of the elongated tubular member or as coating over the rib structure of the elongated tubular member having a central lumen and a flange formed at the proximal end. Such device is formed from the plurality of flexible ribs configured to provide a plurality of seals within the interstitial portion of a fallopian tube and is provided with a valve member within the lumen of the tubular member (*US Patent no. 5,935,137, date of publication 01.04.99*). Such devices also suffer from the disadvantages of being fairly stiff structure and of complicated structure to be fabricated and generally causing injury to the fallopian tube, which may be irreversible in nature and may consequently cause fibrosis. These devices result in permanent sterilization with no scope of reversal of fertility. Further these devices are restricted for use by female only.

Still further class of known contraceptive devices or methods in the art is to affect and/or block the flow of sperms in the vas deferens or ovum in fallopian tube and such contraceptives consists of implantation of a reversible occulusion contraceptive device. Such known devices are generally suitable for contraception or sterilization either of male or of female and not of both.

A class of known surgical contraceptive or occlusion devices, which are suitable for use by male includes an elongated member provided with annular flange (*US Patent no. 3,828,764*), proximal or a distal tube (*US Patent no. 3,990,434*), an elongated hollow tube provided with an elastic cap and a plug (*US Patent no. 4,682,592*), a filament (*US Patent no. 5,471,997*), an expandable body (*Patent application no. WO 97/16132*), urethral sealing member (*US Patent no. 5,603,335*) and urethral occlusive device (*US Patent no. 5,884,629*). The elongated member provided with an annular flange is inserted into severed ends of vas by cutting the vas and sutured to one or both ends of the vas to prevent migration of the device in the vas and is provided by transverse wall to block fluid flow through the vas (*US Patent no. 3,828,764*). The reversibility of fertility is achieved by surgically removing the transverse wall. The proximal tube having a shoulder portion and openings on either end is inserted in the vas after puncturing by hypodermic needle and a distal tube similar in construction to the proximal tube is also inserted in the vas

after making second puncture in the vas along with a closed plug for the prevention of passage of body fluid (*US Patent no. 3,990,434*). The reversibility of fertility is achieved by surgically replacing the closed plug with an open plug. A further development of contraceptive device led to the development of a contraceptive device comprising an elongated hollow tube having an expandable elastic cap forming a fluid tight seal at one end and a plug, including a valve, forming a fluid tight seal at the other end and also a flexible spring within the said tube allows selective ingress and egress of the fluid (*US Patent no. 4,682,592*). This device prevents the transport of sperms by occluding the lumen of vas, the ejaculatory duct or the urethra and is inserted through the urethra. A filament having length at least about one fourth of length of vas and outside diameter about equal to inside diameter of vas and containing an enlargement at one end and is made of a material inert to tissue is inserted in the vas after making an insertion in one wall of vas near the epididymis (*US Patent no. 5,471,997*). This device does not block the passage of the sperms but allow escape of sperms from vas. An expandable body unit having an elastic member, an opening cavity and first, second and third progressively rearwardly spaced cavity regions, a cam member and forwardly extending shaft is inserted into a male urethra penis cavity for blocking the urethra (*Patent Application no. WO 97/16132*). This device is provided with the facility for preventing its successive uses. The containment type inboard contraceptive device including a urethral sealing member in the form of an oblong ring and flexible container bag and a tail or other tensioning means attached to the bag to regulate position of the device is inserted into the urethra in the penis to block sperm passage (*US Patent no. 5,603,335*). The fertility is restored by not using the device. An urethral occlusive device is designed for insertion into male urethral opening (*US Patent no. 5,884,629*).

Another class of known surgical contraceptive or occlusion devices, which are suitable for use by male and female includes multifunctional surgical device (*US Patent no. 4,788,966*), sterilization clip (*US Patent no. 5,193,554*), stent (*US Patent no. 5,474,089*) and an occluding member comprising a tubular framework (*Patent Application no. WO 98/26737*). A multifunctional surgical device is designed to apply an elastic occluding ring onto an anatomical tubular structure or for cutting and cauterizing the cut ends of such a structure or for applying a conventional clip to such a structure (*US Patent no. 4,788,966*). A sterilization clip comprising of an upper and lower jaw made-up of plastic material with capture means for capturing the fallopian tube or vas deferens and

such capture means are provided with soft lining blocks the passage of sperms or ovum by compressing the vas deferens or the fallopian tube (*US Patent no. 5,193,554*). A stent including an expandable section and predetermined portion which is ablatable by application of laser irradiation and such portion includes a guiding segment to guide a fiber optic device or alternately stent includes a collapsible frame structure compressed by a spring, and a central ablatable blocking portion is non-surgically inserted (*US Patent no. 5,474,089*). The reversibility is achieved by applying a laser beam to ablate the portion of the blocking device in order to reopen the duct and to re-establish fertility. An occluding member comprising a tubular framework formed from a shape memory material is configured to be implanted in a reproductive lumen and secured to the wall thereof, alternatively, the occluding member may be collapsed upon a solid plug *(Patent Application no. WO 98/26737)*. The reversibility is achieved by reopening tubular framework by introducing a balloon catheter and by series of inflations of the balloon re-expanding the collapsed occluding member or by removing the plug.

The above two classes of known contraceptive devices and their methods of use, as described herein above for use by male or male and female, suffer from one or more of the disadvantages or limitations. One such disadvantage associated with such know devices and method of use thereof is that such known devices simply act as a blocking device to the passage of sperm and/or ovum. Although contraception or sterilization is obtained for some time, the block also prevents the movement of material other than the sperm and/or ovum as for example water and/or proteins. Hence there is pressure buildup, which may result in damage to the epididymis in the male and ovary in the female. Another disadvantage of such known devices is imperfect blockage, which in turn results in imperfect destruction of the sperm and/or ovum. Still another disadvantage of some of such known devices is that such devices have no anti-sperm and/or anti-ovum action, so sperm and/or ovum leaking past the device when the vas deferens lumen and/or fallopian tube dilates can produce pregnancy. Yet another disadvantage of such known devices is that the use of such devices calls for surgical implantation, which is a cumbersome procedure. Further disadvantage of such known devices is that such devices can get displaced and pregnancy may occur. Still further disadvantage of such known devices is that the restoration of fertility using such devices requires the surgical exploration and hence the success rate will be low. Yet further disadvantage of such known devices is that the initial total blockage leads to rise in anti-sperm antibody titer in the male and

retrograde actum on the ovary in the female, which reduces the chance of actual fertility restoration even when by surgery the device is removed or replaced by another such device for restoring fertility. Still another disadvantage of such known devices is that the insertion into the urethra of some of such devices either permanently, till desired by the patient or temporarily, for each act of intercourse, is painful and likely to produce erosion and infection. Yet another disadvantage of such known devices is that the use of some of such devices requires attention of the user prior and after such intercourse. Further disadvantage associated with such known devices is that the large size of some of such devices leads to rupture of the vas deferens in many cases. Still further disadvantage associated with such known devices is that the use of some of such devices totally destroys a segment of the vas deferens and/or fallopian tube, hence reversal would require special microsurgery to rejoin the vas deferens and/or fallopian tube. Yet further disadvantage associated with such known devices is that the removal of some of such devices becomes difficult and calls for a complicated procedure on account of fibrosis with low success rate.

Yet another class of occlusion methods to achieve contraception or sterilization includes formation of a chemical preparation based plug in the vas deferens and/or fallopian tube, such as formation of polyurethane plug (*UK Patent no. GB2223025*) or neem oil plug (*US Patent no. 5,501,855*) or styrene maleic anhydride copolymer plug (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The polyurethane plug is formed by reacting pre-polymer of polyurethane with a chain-enlargement agent with amino-group under normal atmospheric temperature or above it in the presence of an organic solvent and organic acid catalyst, which is solidified in the ductus deferens (*UK Patent no. GB2223025*). The reversibility is achieved by removal of the plug. The neem oil plug is formed by intra-vas administration of neem oil to male rats, which resulted in blockage of spermatogenesis without affecting the testosterone production (*US Patent no. 5,501,855*). The reversibility has not been achieved. The styrene maleic anhydride copolymer plug is formed by step irradiation of styrene maleic anhydride at a dose of 0.2 to 0.24 megarad for its every 40 gms followed by dissolution in pure dimethyl sulphoxide and thereafter injected into the lumen of the vas deferens (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The reversibility is achieved by flushing of the styrene maleic anhydride copolymer plug by injecting extra dose of pure dimethyl sulphoxide.

The polyurethane plug suffers from similar disadvantages as that of the contraceptive devices for use by male or by male and female, as described herein above.

The neem oil plug preparation has limitation that, it does not polymerise rapidly after injection and hence travels retrograde into the testes. Further, it causes damages to the testes and testicular size reduces. Still further disadvantage of neem oil plug is that the lymph nodes are affected. Yet another limitation of the neem oil plug is that the restoration of fertility is not possible.

The styrene maleic anhydride copolymer plug, herein after referred to as SMA plug, which is undergoing multicentric Phase-III Clinical Trials in India and has been developed by the inventor of the presently disclosed invention, has been observed to have certain limitations, such as, it cannot be detected and/or suitably quantified externally by means of X-ray, CAT scanning, magnetic resonance imaging (MRI) or magnetic field due to the non-radio-opaque nature of the contraceptive drug. Another limitation of SMA plug is that, its spread or distribution in the reproductive tract after injection cannot be controlled. Further limitation of SMA plug is that, for its removal to restore the fertility, another injection of extra dose of dimethyl sulphoxide is required to be given to the patient, hence it cannot be removed from the body conveniently by non-invasive and external means except by using the reversal device disclosed in the *pending Indian Patent application no. 928/DEL/97*, developed by inventor of the present invention. However, the removal of the contraceptive even by this device is not 100% successful due to the difficulty in removal of the contraceptive from the part of vas deferens leading to the prostate region.

The limitations of SMA plug, as described herein above, have also been observed in other similar contraceptive preparations, such as polyurethane plug, neem oil etc., which are intended to be used by male or female or male and female for blockage of the vas deferens and/or fallopian tube by way of formation of plug or for affecting the nature of sperm and/or ovum for achieving the contraception or sterilization, as the basic compound of the such known contraceptive preparations being non-radio-opaque and non-magnetic in character. The MRI also fails to detect the contraceptive mainly due to its poor contrast with the soft tissue. The ultrasound is also incapable of detecting the contraceptive, due to low percentage of the basic compound and inadequate difference of the characteristic impedance from the body tissue. To overcome this disadvantage, if the net percentage of the basic compound is increased, it will have the disadvantages

associated with the higher percentage of such basic compounds. Furthermore, some of the regions of the vas deferens and epididymis are so placed that the ultrasonic approach is not practicable.

Need of the Invention :-

Therefore, there is a need to have a contraceptive, which can overcome all or some of the disadvantages and limitations of the prior art, as described herein above and particularly which is not only reversible in nature but also suitable for male and female subjects and as well as has improved contraceptive action and better controlled delivery, and which necessarily does not require any surgery or flushing of any solvent for its removal from the reproductive duct to restore the fertility but can be removed from the body by non-invasive and external means, and can also be imaged by X-ray, CAT scan, ultrasound, MRI and scanning electrical impedance plethysmography, and the spread or distribution of which can be controlled and quantified within the reproductive tract after injection by external means, further which is required to be injected only once to achieve the contraception.

Objects of the Invention :-

This is the main object of the present invention to make a complete disclosure of an improved injectable reversible contraceptive for use by male as well as by female which is not only reversible in nature but also suitable for male and female subjects and can over come some of the disadvantages and limitations of the prior art, as described herein above.

Another object of this invention is to propose a contraceptive, which has improved contraceptive action as well as more controlled delivery method and reversal action to restore fertility.

Still another object of this invention is to propose a contraceptive, which is capable of imaging by X-ray, CAT scan, ultrasound and MRI, and capable of better control and determination of quantity within the reproductive duct by external means.

Still further an object of the present invention is to disclose a contraceptive which may be detected by scanning electrical impedance plethysmography.

Yet another object of this invention is to propose a contraceptive the spread or distribution of which can be controlled in the reproductive tract after injection by external means.

This is further an object of this invention to disclose a contraceptive which necessarily does not require any surgery or flushing of any solvent for its removal from the reproductive duct to restore the fertility and can be removed from the body by non-invasive and external means.

This is still an object of this invention to disclose a contraceptive, which is required to be injected only once for achieving contraception.

This is yet an object of this invention to disclose a contraceptive which can be reversed by external non-invasive means and necessarily does not require additional injection of an extra dose of the pure solvent, thus avoid the second injection.

This is still further an object of this invention to disclose a contraceptive which not only acts as a blocking agent but also brings about changes in the sperm and/or ovum to result in the contraceptive action, hence overcome the disadvantages associated with the contraceptives capable of acting as blocking agent alone.

Brief Description and Preferred Embodiments of the Invention :-

Accordingly this invention provides a complete disclosure of an improved injectable reversible contraceptive and the method of preparation and use thereof, having above stated characteristics and consisting of contraceptive polymer, a solvent medium, an electrically conducting material and magnetic material, characterised in that the contraceptive polymer is preferably from the hydrogel class of polymers, more preferably a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and the solvent medium is preferably dimethyl sulphoxide solvent, and the electrically conducting material and the magnetic material are essentially taken in the particle forms of microsize and macrosize, particularly it discloses a contraceptive consisting of contraceptive polymer having electrical charge and pH lowering properties, a solvent medium having complexing properties, an electrically conducting material having charge transfer, sperm membrane and ovum covering molecule exchange, and inductive heating properties and magnetic material having magnetising and magnetic force drag properties to achieve the electrical conduction, electrical charge transfer and magnetising properties of the proposed contraceptive. Additionally the size and mechanical consistency of electrically conducting material and magnetic material are so selected that the mechanical characteristic impedance to the passage of ultrasound becomes significantly different from that of body tissue and hence the presence of the contraceptive within the body and its location can be determined by ultrasonography. Furthermore, the quantum of the presently

disclosed contraceptive within the reproductive tract can be determined non-invasively by magnetic field estimations as well as by X-ray imaging, CAT scan, MRI scan and scanning electrical impedance plethysmography.

This is an additional embodiment of the present invention that in order to restore the fertility, that is to remove the contraceptive from the reproductive tract, as and when desired by the subject, the contraceptive is heated by virtue of its electrical properties by electromagnetic induction with fields from outside the body. The heating changes the basic polymer characteristics thereby lowering its contraceptive action to obtain restoration of fertility as and when desired. Further embodiment of this invention includes lowering of viscosity of the contraceptive on induction heating which further facilitates the removal of the preparation from the body by an externally imposed magnetic field, preferably travelling magnetic field so as to restore reproductive functions as and when desired.

Still further embodiment of this invention includes that the swelling and anchoring properties of the presently disclosed contraceptive without adhesion gives long term retention for the contraception with a one time administration. The contraceptive of the presently disclosed invention may also be administered after removal if the person after a period of fertility restoration desires to have contraceptive status.

Yet another embodiment of this invention includes that the contraceptive preparation when placed in the vas deferens or the fallopian tube brings about changes in the sperm and/or ovum to result in contraceptive action. The change is effected by electrical charge properties of the contraceptive polymer; and the charge transfer, and sperm membrane and ovum cover molecule exchange capabilities of the electrically conducting material.

The removal of the contraceptive from the vas deferens or the fallopian tube, in accordance to the preferred embodiment of the present invention is possible by using the magnetic properties of the contraceptive preparation to propel the contraceptive for voiding and restoration of fertility by external magnetic field or alternately is possible by flushing by another injection of the pure solvent. However, reflushing of pure solvent is not intended to restrict the scope of the present invention.

The present invention therefore overcomes the disadvantages and limitations of the class of known contraceptives, which are used in the vas deferens and fallopian tube.

Further, the present invention has the advantage of electrical charge producing and pH lowering polymer, associated with the molecule exchange property and charge transfer property of the electrically conducting material, employed in the presently disclosed contraceptive preparation to greatly minimize the pressure buildup with consequent adverse tissue and immunological changes.

Still further the present invention has the advantage, that the contraceptive is controlled *insitu* by the application of a drag force or a propelling force by means of an external magnetic field. The present invention also discloses the property of residual magnetism in the contraceptive after withdrawal of the external magnetic field. Therefore, the presence of the contraceptive can be detected and to some extent can also be quantified by measuring the residual magnetic field strength from outside the body. Thus a disadvantage of the such known contraceptives that the spread in the reproductive tract after injection cannot be controlled and the presence within the body cannot be suitably located and quantified are overcome by the presently disclosed contraceptive.

Detailed Description of the Invention :-

In accordance with this invention an improved injectable reversible contraceptive and the method of preparation and use thereof is disclosed wherein the base compound is a contraceptive polymer, which can generate an electrical charge when in contact with body water. A range of polymers can be used and a preferred class of polymers is the hydrogel class, which swells and invaginates into the folds of the lumen to help retention but does not adhere to tissue thereby allowing scope for removal. Among the hydrogel class of polymers several different polymers may be used, however the mixture of styrene maleic anhydride and styrene maleic acid copolymers is the most preferred option. In accordance to the preferred embodiment of this invention the styrene maleic anhydride and styrene maleic acid copolymers are first mixed and then dissolved in the solvent medium, preferably dimethyl sulphoxide solvent or alternately are directly dissolved in the solvent medium followed by mixing. An additive, herein referred as electrically conducting material is added to the contraceptive formulation to obtain electrical conductivity and charge transfer capabilities of the presently disclosed contraceptive. In accordance to the preferred embodiment of this invention the electrically conducting material is preferably copper in its pure form consisting of microsize particle and macrosize particle. The electrically conducting material, preferably the copper particles, as employed in the presently disclosed contraceptive, besides giving electrical conductivity also enhances the

active property of the contraceptive polymer, herein referred as base polymer, to affect the structure of the sperm and the ovum by displacing some specific molecules from the sperm, for example zinc and ovum, for example proteins. In accordance to one of embodiments of this invention, when an external time varying magnetic field is applied there is electromagnetic induction and the copper particles of the presently disclosed contraceptive get hot. A microwave field is very effective in this respect and can change the polymer constitution as well as viscosity. Another additive, herein referred as magnetic material, is added to the polymer to impart the magnetic properties to the presently disclosed contraceptive. In accordance to the preferred embodiment of the present invention, magnetic material is iron in pure form or in the form of oxide or a combination with copper or with a biologically accepted material like sulphur, more preferably magnetic material is iron in its pure form consisting of microsize particle and macrosize particle. In accordance to this invention the above stated additives are uniformly dispersed in the base polymer and the aggregation of the magnetic material, preferably iron particles is prevented by suitable coating, which is preferably of cross-linked styrene maleic anhydride copolymer.

The particle size as well as the percentage by weight with respect to the contraceptive polymer of both the materials, that is electrically conducting material and magnetic material are so selected that the contraceptive action as well as the propelling functions of the contraceptive are achieved adequately. In addition these factors are controlled so that the mechanical properties at frequency of 1 to 60 MHz become significantly different from body tissue to be able to distinguish the contraceptive by its ultrasound reflection and refraction properties. Further on account of the electrical conductive property on passage of a low level alternating current the electrical impedance offered by the contraceptive preparation of this invention within the reproductive tubes will be different from that of the surrounding tissues, hence the presence of the presently disclosed contraceptive may be detected by scanning electrical impedance plethysmography also.

In accordance to the presently disclosed invention the particle size of microsize particles of electrically conducting material is about 0.005 to 20μ, preferably about 0.5 to 15μ and of macrosize particles of electrically conducting material is about 150μ to 0.2mm. Further, the particle size of microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of macrosize particles of magnetic material is upto

0.5mm. In accordance to this invention the microsize and macrosize particles of electrically conducting material are taken approximately in equal amounts by weight, and the microsize particles of magnetic material are taken in lower amount as compared to the macrosize particles of magnetic material. Further, in accordance with the present invention the quantum of electrically conducting material and magnetic material each varies between 3 to 20% by weight of the contraceptive polymer, particularly the electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of contraceptive polymer and magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of the contraceptive polymer.

In accordance to this invention the styrene maleic anhydride copolymer is prepared by the process known in the art or as disclosed in the *US Patent no. 5,488,075 and Indian Patent no. 183196* of the present inventor. The styrene maleic acid copolymer is prepared from styrene maleic anhydride copolymer either by the process known in the art or by the process disclosed herein after. For preparation of styrene maleic acid copolymer about 0.5gms of styrene maleic anhydride copolymer is taken in a round or flat bottom flask. About 50ml of about 0.5N NaOH is added to this amount of styrene maleic anhydride copolymer. The solution is left for refluxing for about 8 hrs. The refluxed material is allowed to cool down to ambient temperature followed by neutralisation with about 0.5N HCl till white precipitates of styrene maleic acid copolymer are formed. The precipitates of styrene maleic acid copolymer are separated and washed with distilled water and dried in vacuum. It is assured that styrene maleic anhydride copolymer and styrene maleic acid copolymer are free from their respective monomers.

In accordance to this invention, the presently disclosed contraceptive is prepared by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in the solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of the copolymers, the electrically conducting material and the magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C. The magnetic material is preferably the coated magnetic material to avoid aggregation of the magnetic particles. In accordance to preferred embodiment of this invention the copolymers, and the electrically conducting material and magnetic material are first mixed and then dissolved in the solvent.

Alternately, the copolymers, and the electrically conducting material and magnetic material are directly dissolved in the solvent followed by mixing. In accordance to another preferred embodiment of this invention the copolymers are first mixed and then dissolved in the solvent followed by addition of the electrically conducting material and magnetic material. The electrically conducting material and the magnetic material are added either together or one after the other.

According to the preferred embodiment of this invention, the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material are first mixed together and then dissolved in about 99% pure dimethyl sulphoxide. Such manner of mixing assures the uniform distribution of particles of electrically conducting and magnetic materials.

In accordance to one of the preferred embodiments of this invention, the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material are directly dissolved in the solvent, preferably in about 99% pure dimethyl sulphoxide followed by mixing.

In accordance to one of the preferred embodiments of the present invention weighed quantities of styrene maleic anhydride copolymer and styrene maleic acid copolymer are first mixed and then dissolved in a solvent. To this complexed solution of contraceptive polymer and solvent medium weighed quantities of electrically conducting material and of coated magnetic material are added.

In accordance to the preferred embodiment of the present invention the weighed quantities of electrically conducting material and of magnetic material are added either together or one after the other.

In accordance to this invention the weighed ratios of styrene maleic anhydride copolymer and styrene maleic acid copolymer may be selected over a wide range to suit the specific need in terms of time period for onset of contraceptive action, duration of contraceptive action and extent of intervention required for reversal. Particularly, the ratio of styrene maleic acid copolymer and styrene maleic anhydride copolymer with respect to each other varies between 1.5:8.5 to 3:7, preferably 2:8. The scope of the present invention is not limited by the molecular weight of styrene maleic anhydride copolymer or styrene maleic acid copolymer.

Experimentally, the contraceptive of the presently disclosed invention can be prepared by mixing 70% of styrene maleic anhydride copolymer, 15% of styrene maleic

acid copolymer, 5% of electrically conducting material and 10% of magnetic material and dissolving this mixed composition in about 99% pure dimethyl sulphoxide in the ratio in a manner that for every 100mg of the contraceptive polymer, that is for every 100mg of mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer about 200µl of dimethyl sulphoxide is added. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting and coated magnetic materials in the solvent is kept in nitrogen atmosphere and shaken for about 47 hrs by maintaining the temperature at about 35^0C. The resulting viscous contraceptive preparation is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

In accordance to another experiment of the present invention, 80mg of styrene maleic anhydride copolymer, 20mg of styrene maleic acid copolymer, 5mg of 99.9% pure copper particles consisting of microsize and macrosize particles and 10mg of coated iron particles consisting of microsize and macrosize particles are mixed with 200µl of about 99% pure dimethyl sulphoxide. The particle sizes of copper and iron particles are maintained within the limits described herein above. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, copper particles and coated iron particles in dimethyl sulphoxide is kept in nitrogen atmosphere and shaken for about 48 hrs by maintaining the temperature at 35^0C. The resulting viscous contraceptive preparation is ready for injection to the desired male or female and is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

The contraceptive of the present invention can be injected in male or female by any known means. However, specially designed process is described herein after merely for understanding and not to limit the scope of this invention. This described process is to take care of the specially embodied properties, particularly the charge transfer, electrical and magnetic properties of the presently disclosed contraceptive. In accordance to the preferred embodiment of the present invention the contraceptive preparation is taken in 250µl syringe, which is provided with about 23gauge needle.

In the male a puncture is made in the middle of the anterior surface of the scrotum, through which a small segment of vas deferens of the left side is delivered without injuring the vas deferens. This procedure is referred as 'no scalpel' procedure. Applying compression with the fingers onto the proximal portion of the vas deferens, that is towards

the testis, the needle is inserted into lumen of the vas deferens with the needle pointing distally, that is towards the ejaculatory duct. The planned amount of the drug, which is guided by various factors, such as time period for onset of contraceptive action, duration of contraceptive action and extent of intervention required for reversal, as described herein above, is injected and typically the dose is 120µl. In order to control the distribution of the contraceptive a strong electromagnet with field strength of above 2500 gauss is placed over the surface marking the inguinal canal a little distally than the external inguinal ring. The vas deferens is then allowed to slip back into the scrotum through the scrotal puncture hole and the vas of the other side is delivered through the same hole and the procedure is repeated. The advantage of this procedure is that no suturing of the puncturing hole is required and only a strip of tape is placed over puncture hole. The subject is advised not to have sexual activity during next 72 hrs following the injection.

In accordance to the present invention the injected contraceptive can also be reversed at any desired time for restoration of fertility without any requirement of surgery or flushing of an extra dose of the solvent. Therefore, for reversal of the contraceptive action to restore the fertility, the vas deferens in the scrotal segment is palpated in a special manner to propel the contraceptive preparation into the inguinal segment of the vas deferens. By applying radio frequency diathermy energy from outside the body electrical currents are induced in the electrical conducting particles in the contraceptive causing heating of the contraceptive, softening of the contraceptive and some molecular breakdown. A strong DC electromagnet is rapidly moved over the body surface parallel to the surface marking the spermatic cord, which contains the vas deferens. Alternately, a travelling electromagnetic field is applied and moved over the pelvic region and the procedures are repeated to propel the contraceptive into the ampulla of the vas deferens. Finally with the finger inserted into the rectum via the anus the ampulla of the vas deferens is squeezed to expel the contraceptive into the ejaculatory duct.

In the female the contraceptive is injected into the fallopian tube also known as the oviduct via the ostium. The ostium is the junction of the fallopian tube and the uterus. The site is approached via the vagina and the uterine cervical canal. A hysteroscope is used to visualize the ostium. Since the syringe with the drug is kept outside the body a length of the tubing of about 16 gauge is connected to the syringe. A strong DC permanent magnet or an electromagnet is placed on the abdominal surface such that the field is directed towards the uterus. The field will check the travel of the contraceptive and spillage of the

contraceptive into the peritoneal cavity. A hysteroscope is inserted via the vagina and the cervical canal so that the ostium is viewed. The tubing from the syringe is passed via a channel of the hysteroscope so that the tip of the catheter enters the fallopian tube through the ostium. From the syringe the contraceptive is injected into the fallopian tube. Typically 100µl of the contraceptive is injected into one fallopian tube. After injecting into the fallopian tube on one side the hysteroscope is shifted to view the ostium on the other side and advancing the tube the same amount of the contraceptive is injected into the fallopian tube.

In accordance to the present invention the injected contraceptive can also be reversed at any desired time for restoration of fertility without any requirement of surgery or flushing of an extra dose of the solvent. Therefore, for reversal of the contraceptive action to restore the fertility, a radio frequency field is applied to the body to cause induction in the electrical particles and raise the temperature of the particles. A strong DC permanent magnet is moved over the body surface parallel to the fallopian tube so as to propel the contraceptive towards the uterus. Additionally by means of a catheter a suction is applied at the ostium to draw out the contraceptive.

Claims

1. An improved injectable reversible contraceptive comprising a contraceptive polymer, a solvent medium, an electrically conducting material and magnetic material, characterised in that said contraceptive polymer is preferably from the hydrogel class of polymers, more preferably mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and said solvent medium is preferably dimethyl sulphoxide solvent, and said electrically conducting material and said magnetic material are essentially taken in particle forms of microsize and macrosize.

2. A contraceptive as claimed in claim 1, wherein styrene maleic acid copolymer and styrene maleic anhydride copolymer are taken in the ratio varying between 1.5:8.5 to 3:7, preferably 2:8 with respect to each other.

3. A contraceptive as claimed in claim 1, wherein said electrically conducting material is preferably copper in its pure form consisting of microsize particle and macrosize particle.

4. A contraceptive as claimed in claim 1, wherein said magnetic material is iron in pure form or in the form of oxide or a combination with copper or with a biologically accepted material like sulphur, more preferably magnetic material is iron in its pure form consisting of microsize particle and macrosize particle.

5. A contraceptive as claimed in claim 1, wherein said electrically conducting material and said magnetic material each varies between 3 to 20% by weight of said contraceptive polymer.

6. A contraceptive as claimed in claims 1 and 5, wherein said electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of said contraceptive polymer.

7. A contraceptive as claimed in claims 1 and 5, wherein said magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of said contraceptive polymer.

8. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of said electrically conducting material is about 0.005 to 20μ, preferably about 0.5 to 15μ and of said macrosize particles of said electrically conducting material is about 150μ to 0.2mm.

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 μl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claims 1 and 13, wherein said magnetic material is preferably coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body.

16. A contraceptive as claimed in claim 1, characterised in that the viscosity of the contraceptive is lowered on induction heating by an externally imposed electro-magnetic field.

17. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

18. A contraceptive as claimed in claim 1, characterised in that the contraceptive is controlled *insitu* by the application of a drag force or a propelling force by means of an external magnetic field.

19. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

20. A contraceptive as claimed in claim 1, characterised in that the flow of the contraceptive after injection is controlled by external means.

21. A contraceptive as claimed in claims 1 and 20, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

22. An improved injectable reversible contraceptive as claimed in claims 1 to 21 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 20 to 28 and substantially described herein above.

AMENDED CLAIMS

[received by the International Bureau on 25 August 2000 (25.08.00);
original claims 15 - 22 replaced by amended claims 15 - 20,
remaining claims unchanged (2 pages)]

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 μl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claims 1 and 13, wherein said magnetic material is preferably coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

16. A contraceptive as claimed in claims 1 or 15, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body, which in-turn causes lowering in viscosity of said contraceptive to effect the reversal thereof.

17. A contraceptive as claimed in claim 1, characterised in that the *in-situ* flow of the contraceptive after injection is controlled by external means, preferably by the application of a drag force or a propelling force by means of an external magnetic field.

18. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

19. A contraceptive as claimed in claims 1 or 18, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

20. An improved injectable reversible contraceptive as claimed in claims 1 to 19 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^{0}C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 20 to 28 and substantially described herein above.

STATEMENT UNDER ARTICLE 19 (1)

Originally **International / PCT Patent Application [No. PCT/IN 00/00023]** had 29 claims and now, after amendments by way of merging some claims, there are 27 claims. Original claims 1 to 14 and claims 23 to 29 are unchanged. Original claim 17 and 19 are also unchanged but amendments have necessitated their renumbering as claim 15 and 18 respectively. Original claims 15 and 16 are merged and are replaced by amended claim 16. Original claims 18 and 20 are also merged and are replaced by amended claim 17. Original claims 21 and 22 are replaced by amended claims 19 and 20 respectively. No new claim has been added.

The amended claims will not have any impact on the description as the amended claims do not go beyond the scope of the originally filed patent application.

ESTABLISHED 1827

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RKM/IP : PCT/IN 00/00023

February 26, 2001

By FAX NO. 49-89-2399-4465
Confirmation by Courier

International Preliminary Examination Authority (IPEA)
European Patent Office
Erhardtstr. 27
D-80298
MUNICH
GERMANY

KIND ATTN. : A. Hedegaard, Esqr., Examiner

Dear Sirs,

Reference : **International Preliminary Examination of**
PCT/International Patent Application No. PCT/IN 00/00023
International Filing Date : March 16, 2000 [16/03/2000]
Priority Date : March 17, 1999 [17/03/1999]
Agent's File Reference No. IN/PA267/SKG
Applicant : GUHA, Sujoy, Kumar
In Chapter II – International Phase

With reference to your first written opinion of December 27, 2000 under PCT Rule 66 in respect of the above identified PCT application, a written reply under PCT Rule 66.3 along with amended sheet nos. 8, 9, 11, 12, 15 and 17 of the description, and claim pages 20-22, and abstract page 23 as amended under Article 34 are enclosed herewith.

Originally this PCT application had 27 claims (excluding claims 21 and 22 deleted under Article 19) and now, after amendments by way of merging and deleting some claims, there are 26 claims. Original claim 3 has been merged with claim 1 and hence indicated as deleted. Original claims 1, 4, 6, 7, 14, 20 and 29 have been amended and other claims are unchanged. No new claim has been added.

Applicant earnestly requests that this response be fully considered before establishing the international preliminary examination report.

If there is any further opinion, applicant would appreciate receiving the same by FAX NO. 011-5594437/5598013. Applicant would also appreciate for an

additional opportunity to submit the response and amendments, if required to such further opinion.

The acknowledgment of receipt of this letter along with enclosures thereto will be highly appreciated.

Thanking you,

Yours faithfully,

(Dr. Ramesh Kumar MEHTA)
Of REMFRY & SAGAR
PATENT ATTORNEYS FOR THE APPLICANT

Enclosures : Response to the written opinion – three pages;
Amended sheet nos. 8, 9, 11, 12, 15 and 17 of the description;
Amended claim pages 20-22; and
Amended abstract page 23

Total no. of pages – Fifteen (including two pages of this letter)

IN THE EUROPEAN PATENT OFFICE, MUNICH
PCT APPLICATION

APPLICANT	: GUHA, Sujoy, Kumar
International Appn. No.	: PCT/IN 00/00023
International Filing date	: 16/03/2000
Priority Date	: 17/03/1999
Title	: An Improved Reversible Contraceptive for Male and Female

WRITTEN REPLY TO THE FIRST WRITTEN OPINION

European Patent Office
D-80298
MUNICH
Fax No. 49 89 2399 4465

Kind Attention : A. Hedegaard, Esqr.
Examiner

In accordance with PCT Rule 66.3, this is a written reply to the first written opinion of 27 December 2000 (27/12/2000).

The written opinion (paragraph III) states that claims 20 and 29 due to the feature "substantially described hereinabove" are so unclear that no meaningful opinion could be formed.

Applicant respectfully submits that the claims with such features are known as "omnibus claims" in some of the PCT member countries including India (IN), wherein such claims are allowed. Therefore, applicant requests that these claims with these features be allowed to remain in the PCT application for protection in some of the PCT member countries, like India (IN).

The written opinion (paragraph V) states that claim 1 is not novel and claim 23 is novel but does not involve an inventive step in view of the cited document – D1.

Applicant respectfully submits that the D1 discloses a contraceptive, which comprises "nylon", "ethanol" and "Cu-Zn alloys" as contraceptive polymer, solvent and electrically conducting material respectively in addition to "phenol and glycerol" as against "hydrogel class of polymers, particularly a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer", "dimethyl sulfoxide", "pure copper (Cu) particles" and "pure iron (Fe) particles" as a contraceptive polymer, a solvent, an electrically conducting material and a magnetically conducting material in the present invention [please refer at amended sheet no. 11, lines 16 to 23 of the PCT application].

It is clear from the above submission that D1 does not comprise a "magnetically conducting material", but comprises "Cu-Zn alloys", known as "pinchbeck alloy", which are not magnetic, therefore this contraceptive formulation is "non-

magnetic" in nature as against "magnetic contraceptive" of the present invention. Therefore, the contraceptive of D1 can not be propelled by means of external magnetic field. In contrast, the contraceptive of this invention can be propelled by means of the external magnetic field. These magnetic properties along with the electrical properties of the contraceptive of the present invention make it "reversible contraceptive" to restore fertility by means of external magnetic field as and when desired by the subject. Further, the delivery, spread, distribution and *in-situ* flow of this contraceptive can be detected, controlled and quantified by external means. [please refer to objects and brief description, particularly at page 12, lines 4 to 13 of the PCT application]. It may further be noted that the D1 contraceptive comprises Zn in the form of Cu-Zn alloys. In contrast, the contraceptive of this invention displaces zinc (Zn) from the sperm etc. for achieving the specific properties as described in the description [please refer at page 13, lines 32-33 and at page 14, lines 1-3 of PCT application].

Further, the contraceptive of D1 is a "blocking device" for blocking the oviduct or vas deferens and such a contraceptive acts as "adhesion-blocker" as admitted by the inventor in the title and the abstract of D1. In contrast, the contraceptive of this invention acts not only as a blocking agent but also brings about changes in the sperms and/or ovum to result in the contraceptive action which happens due to the presence of said polymer mixture and pure Cu particles as electrically conducting material [please refer at page 11, lines 10-14 and lines 23-27; at page 12, lines 19-24; at page 13, lines 32-33 and at page 14, lines 1-3 of PCT application]. However, the blocking action is not permanent, therefore, this contraceptive is reversible in nature. Further, applicant discloses a contraceptive which does not has "adhesion properties" and still has long term retention properties for contraception with one time administration [please refer at page 12, lines 14-18 of PCT application].

Further, applicant recites the limitation that Cu and Fe essentially consist of microsize and macrosize particles. The purpose of having the contraceptive with these particles is stated at page 11, lines 29-33 of the PCT application.

The difference in the properties of the D1 contraceptive and the contraceptive of the present application is caused by the difference in their respective composition. Further, such properties/effects of the presently disclosed contraceptive could not be foreseen or expected by a person skilled in the art from reading of the cited document (D1) either alone or in combination with any other document.

As desired, the term "preferable" has been deleted in claim 1. The description has been brought into conformity with the new claims being filed. It is certified that the revised description and claims neither disclose and claim any new subject-matter nor add subject-matter which extends beyond the content of the PCT application as published.

In light of the above submissions, the claim 1 is novel and claim 23 involves an inventive step over the prior art cited (D1).

The written opinion (paragraph VII) states that reference to D1 should be mentioned in the description. Applicant has made a mention of D1 on amended sheet no. 8; lines 18 and 24-25 and on amended sheet no. 9, lines 1-2 of the PCT application.

The written opinion (paragraph VIII) states that the words "about", "approximately" and "improved" should be deleted throughout the claims.

Applicant respectfully submits that such words are allowed under prevailing practice in some of the PCT member countries. The words "about" and "approximately" indicate permissible variations in the values and ranges of the ingredients and process parameters, and such variations are well known in the art. Therefore, applicant earnestly requests that such words may kindly be allowed to remain in view of the prevailing practice in some of the PCT member countries. However, the word "improved" has been deleted in the claims. Applicant respectfully submits that this word may be allowed to remain in the title and description of the PCT application to indicate that the presently disclosed contraceptive is an improved version over the prior art.

The phrase "not intended to restrict/limit the scope of the invention" has been deleted and amended sheet nos. 12 and 17 are enclosed.

The revision has necessitated retyping of pages 8, 9, 11, 12, 15 and 17 of the description, and claim pages 20-22, and abstract page 23. The amended sheets are enclosed herewith.

Applicant earnestly requests that this response be fully considered before establishing the international preliminary examination report.

Respectfully submitted,

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Dated 26 February, 2001 (26/02/01)

retrograde actum on the ovary in the female, which reduces the chance of actual fertility restoration even when by surgery the device is removed or replaced by another such device for restoring fertility. Still another disadvantage of such known devices is that the insertion into the urethra of some of such devices either permanently, till desired by the patient or temporarily, for each act of intercourse, is painful and likely to produce erosion and infection. Yet another disadvantage of such known devices is that the use of some of such devices requires attention of the user prior and after such intercourse. Further disadvantage associated with such known devices is that the large size of some of such devices leads to rupture of the vas deferens in many cases. Still further disadvantage associated with such known devices is that the use of some of such devices totally destroys a segment of the vas deferens and/or fallopian tube, hence reversal would require special microsurgery to rejoin the vas deferens and/or fallopian tube. Yet further disadvantage associated with such known devices is that the removal of some of such devices becomes difficult and calls for a complicated procedure on account of fibrosis with low success rate. Yet another class of occlusion methods to achieve contraception or sterilization includes formation of a chemical preparation based plug in the vas deferens and/or fallopian tube, such as formation of polyurethane plug (*UK Patent no. GB2223025*) or nylon plug (CN 85108504A) or neem oil plug (*US Patent no. 5,501,855*) or styrene maleic anhydride copolymer plug (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The polyurethane plug is formed by reacting pre-polymer of polyurethane with a chain-enlargement agent with amino-group under normal atmospheric temperature or above it in the presence of an organic solvent and organic acid catalyst, which is solidified in the ductus deferens (*UK Patent no. GB2223025*). The reversibility is achieved by removal of the plug. The nylon plug is formed by reacting nylon, EtOH, phenol, Cu-Zn alloys and glycerol which also results in blockage of oviduct or vas deference (CN85108504). The neem oil plug is formed by intra-vas administration of neem oil to male rats, which resulted in blockage of spermatogenesis without affecting the testosterone production (*US Patent no. 5,501,855*). The reversibility has not been achieved. The styrene maleic anhydride copolymer plug is formed by step irradiation of styrene maleic anhydride at a dose of 0.2 to 0.24 megarad for its every 40 gms followed by dissolution in pure dimethyl sulphoxide and thereafter injected into the lumen of the vas deferens (*US Patent no. 5,488,075 and Indian Patent no. 183196*). The reversibility is achieved by flushing of the styrene maleic anhydride copolymer plug by injecting extra dose of pure dimethyl

sulphoxide. The polyurethane and nylon plugs suffer from similar disadvantages as that of the contraceptive devices for use by male or by male and female, as described herein above. The neem oil plug preparation has limitation that, it does not polymerise rapidly after injection and hence travels retrograde into the testes. Further, it causes damages to the testes and testicular size reduces. Still further disadvantage of neem oil plug is that the lymph nodes are affected. Yet another limitation of the neem oil plug is that the restoration of fertility is not possible.

The styrene maleic anhydride copolymer plug, herein after referred to as SMA plug, which is undergoing multicentric Phase-III Clinical Trials in India and has been developed by the inventor of the presently disclosed invention, has been observed to have certain limitations, such as, it cannot be detected and/or suitably quantified externally by means of X-ray, CAT scanning, magnetic resonance imaging (MRI) or magnetic field due to the non-radio-opaque nature of the contraceptive drug. Another limitation of SMA plug is that, its spread or distribution in the reproductive tract after injection cannot be controlled. Further limitation of SMA plug is that, for its removal to restore the fertility, another injection of extra dose of dimethyl sulphoxide is required to be given to the patient, hence it cannot be removed from the body conveniently by non-invasive and external means except by using the reversal device disclosed in the *pending Indian Patent application no. 928/DEL/97*, developed by inventor of the present invention. However, the removal of the contraceptive even by this device is not 100% successful due to the difficulty in removal of the contraceptive from the part of vas deferens leading to the prostate region.

The limitations of SMA plug, as described herein above, have also been observed in other similar contraceptive preparations, such as polyurethane plug, neem oil etc., which are intended to be used by male or female or male and female for blockage of the vas deferens and/or fallopian tube by way of formation of plug or for affecting the nature of sperm and/or ovum for achieving the contraception or sterilization, as the basic compound of the such known contraceptive preparations being non-radio-opaque and non-magnetic in character. The MRI also fails to detect the contraceptive mainly due to its poor contrast with the soft tissue. The ultrasound is also incapable of detecting the contraceptive, due to low percentage of the basic compound and inadequate difference of the characteristic impedance from the body tissue. To overcome this disadvantage, if the net percentage of the basic compound is increased, it will have the disadvantages

This is further an object of this invention to disclose a contraceptive which necessarily does not require any surgery or flushing of any solvent for its removal from the reproductive duct to restore the fertility and can be removed from the body by non-invasive and external means. This is still an object of this invention to disclose a contraceptive, which is required to be injected only once for achieving contraception.

This is yet an object of this invention to disclose a contraceptive which can be reversed by external non-invasive means and necessarily does not require additional injection of an extra dose of the pure solvent, thus avoid the second injection.

This is still further an object of this invention to disclose a contraceptive which not only acts as a blocking agent but also brings about changes in the sperm and/or ovum to result in the contraceptive action, hence overcome the disadvantages associated with the contraceptives capable of acting as blocking agent alone.

Brief Description and Preferred Embodiments of the Invention :-

Accordingly this invention provides a complete disclosure of an injectable reversible contraceptive and the method of preparation and use thereof, having above stated characteristics and consisting of contraceptive polymer, a solvent medium, an electrically conducting material and a magnetic material, characterised in that the contraceptive polymer is from the hydrogel class of polymers, particularly a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and the solvent medium is dimethyl sulphoxide solvent, and the electrically conducting material is copper in its pure form essentially consisting of microsize particles and macrosize particles, and the magnetic material is iron in its pure form essentially consisting of microsize particles and macrosize particles, particularly it discloses a contraceptive consisting of contraceptive polymer having electrical charge and pH lowering properties, a solvent medium having complexing properties, an electrically conducting material having charge transfer, sperm membrane and ovum covering molecule exchange, and inductive heating properties and magnetic material having magnetising and magnetic force drag properties to achieve the electrical conduction, electrical charge transfer and magnetising properties of the proposed contraceptive. Additionally the size and mechanical consistency of electrically conducting material and magnetic material are so selected that the mechanical characteristic impedance to the passage of ultrasound becomes significantly different from that of body tissue and hence the presence of the contraceptive within the body and its location can be determined by ultrasonography. Furthermore, the quantum of the presently

disclosed contraceptive within the reproductive tract can be determined non-invasively by magnetic field estimations as well as by X-ray imaging, CAT scan, MRI scan and scanning electrical impedance plethysmography.

This is an additional embodiment of the present invention that in order to restore the fertility, that is to remove the contraceptive from the reproductive tract, as and when desired by the subject, the contraceptive is heated by virtue of its electrical properties by electromagnetic induction with fields from outside the body. The heating changes the basic polymer characteristics thereby lowering its contraceptive action to obtain restoration of fertility as and when desired. Further embodiment of this invention includes lowering of viscosity of the contraceptive on induction heating which further facilitates the removal of the preparation from the body by an externally imposed magnetic field, preferably travelling magnetic field so as to restore reproductive functions as and when desired.

Still further embodiment of this invention includes that the swelling and anchoring properties of the presently disclosed contraceptive without adhesion gives long term retention for the contraception with a one time administration. The contraceptive of the presently disclosed invention may also be administered after removal if the person after a period of fertility restoration desires to have contraceptive status.

Yet another embodiment of this invention includes that the contraceptive preparation when placed in the vas deferens or the fallopian tube brings about changes in the sperm and/or ovum to result in contraceptive action. The change is effected by electrical charge properties of the contraceptive polymer; and the charge transfer, and sperm membrane and ovum cover molecule exchange capabilities of the electrically conducting material.

The removal of the contraceptive from the vas deferens or the fallopian tube, in accordance to the preferred embodiment of the present invention is possible by using the magnetic properties of the contraceptive preparation to propel the contraceptive for voiding and restoration of fertility by external magnetic field or alternately is possible by flushing by another injection of the pure solvent.

The present invention therefore overcomes the disadvantages and limitations of the class of known contraceptives, which are used in the vas deferens and fallopian tube.

0.5mm. In accordance to this invention the microsize and macrosize particles of electrically conducting material are taken approximately in equal amounts by weight, and the microsize particles of magnetic material are taken in lower amount as compared to the macrosize particles of magnetic material. Further, in accordance with the present invention the quantum of electrically conducting material and magnetic material each varies between 3 to 20% by weight of the contraceptive polymer, particularly the electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of contraceptive polymer and magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of the contraceptive polymer.

In accordance to this invention the styrene maleic anhydride copolymer is prepared by the process known in the art or as disclosed in the *US Patent no. 5,488,075 and Indian Patent no. 183196* of the present inventor. The styrene maleic acid copolymer is prepared from styrene maleic anhydride copolymer either by the process known in the art or by the process disclosed herein after. For preparation of styrene maleic acid copolymer about 0.5gms of styrene maleic anhydride copolymer is taken in a round or flat bottom flask. About 50ml of about 0.5N NaOH is added to this amount of styrene maleic anhydride copolymer. The solution is left for refluxing for about 8 hrs. The refluxed material is allowed to cool down to ambient temperature followed by neutralisation with about 0.5N HCl till white precipitates of styrene maleic acid copolymer are formed. The precipitates of styrene maleic acid copolymer are separated and washed with distilled water and dried in vacuum. It is assured that styrene maleic anhydride copolymer and styrene maleic acid copolymer are free from their respective monomers.

In accordance to this invention, the presently disclosed contraceptive is prepared by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in the solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of the copolymers, the electrically conducting material and the magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C. The magnetic material is coated magnetic material to avoid aggregation of the magnetic particles. In accordance to preferred embodiment of this invention the copolymers, and the electrically conducting material and magnetic material are first mixed and then dissolved in the solvent.

acid copolymer, 5% of electrically conducting material and 10% of magnetic material and dissolving this mixed composition in about 99% pure dimethyl sulphoxide in the ratio in a manner that for every 100mg of the contraceptive polymer, that is for every 100mg of mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer about 200µl of dimethyl sulphoxide is added. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting and coated magnetic materials in the solvent is kept in nitrogen atmosphere and shaken for about 47 hrs by maintaining the temperature at about 35^0C. The resulting viscous contraceptive preparation is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

In accordance to another experiment of the present invention, 80mg of styrene maleic anhydride copolymer, 20mg of styrene maleic acid copolymer, 5mg of 99.9% pure copper particles consisting of microsize and macrosize particles and 10mg of coated iron particles consisting of microsize and macrosize particles are mixed with 200µl of about 99% pure dimethyl sulphoxide. The particle sizes of copper and iron particles are maintained within the limits described herein above. This complex solution of styrene maleic anhydride copolymer, styrene maleic acid copolymer, copper particles and coated iron particles in dimethyl sulphoxide is kept in nitrogen atmosphere and shaken for about 48 hrs by maintaining the temperature at 35^0C. The resulting viscous contraceptive preparation is ready for injection to the desired male or female and is placed in the syringe for injection while ensuring that atmospheric air and moisture do not come in contact with the contraceptive preparation.

The contraceptive of the present invention can be injected in male or female by any known means. However, specially designed process is described herein after merely for understanding. This described process is to take care of the specially embodied properties, particularly the charge transfer, electrical and magnetic properties of the presently disclosed contraceptive. In accordance to the preferred embodiment of the present invention the contraceptive preparation is taken in 250µl syringe, which is provided with about 23gauge needle.

In the male a puncture is made in the middle of the anterior surface of the scrotum, through which a small segment of vas deferens of the left side is delivered without injuring the vas deferens. This procedure is referred as 'no scalpel' procedure. Applying compression with the fingers onto the proximal portion of the vas deferens, that is towards

Claims

1. An injectable reversible contraceptive comprising a contraceptive polymer, a solvent medium, an electrically conducting material and a magnetic material, characterised in that said contraceptive polymer is from the hydrogel class of polymers, particularly a mixture of styrene maleic anhydride copolymer and styrene maleic acid copolymer, and said solvent medium is dimethyl sulphoxide solvent, and said electrically conducting material is copper in its pure form essentially consisting of microsize particles and macrosize particles, and said magnetic material is iron in its pure form essentially consisting of microsize particles and macrosize particles.

2. A contraceptive as claimed in claim 1, wherein styrene maleic acid copolymer and styrene maleic anhydride copolymer are taken in the ratio varying between 1.5:8.5 to 3:7, preferably 2:8 with respect to each other.

3. Deleted.

4. A contraceptive as claimed in claim 1, wherein said magnetic material is iron in the form of oxide or a combination with a biologically accepted material, like sulphur, essentially consisting of microsize particles and macrosize particles.

5. A contraceptive as claimed in claim 1, wherein said electrically conducting material and said magnetic material each varies between 3 to 20% by weight of said contraceptive polymer.

6. A contraceptive as claimed in claim 5, wherein said electrically conducting material is taken between 3-8%, preferably between 4-6%, more preferably about 5% by weight of said contraceptive polymer.

7. A contraceptive as claimed in claim 5, wherein said magnetic material is taken between 6-15%, preferably between 8-12%, more preferably about 10% by weight of said contraceptive polymer.

8. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of said electrically conducting material is about 0.005 to 20μ, preferably about 0.5 to 15μ and of said macrosize particles of said electrically conducting material is about 150μ to 0.2mm.

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 µl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claim 13, wherein said magnetic material is coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

16. A contraceptive as claimed in claims 1 or 15, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body, which in-turn causes lowering in viscosity of said contraceptive to effect the reversal thereof.

17. A contraceptive as claimed in claim 1, characterised in that the *in-situ* flow of the contraceptive after injection is controlled by external means, preferably by the application of a drag force or a propelling force by means of an external magnetic field.

18. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

19. A contraceptive as claimed in claims 1 or 18, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

20. An injectable reversible contraceptive as claimed in claims 1 to 19 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid

copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 23 to 28 and substantially described herein above.

Abstract

The present invention relates to an injectable reversible contraceptive for use by male and female comprising a contraceptive polymer, a solvent medium, an electrically conducting material and a magnetic material, characterised in that the contraceptive polymer is a mixture of styrene maleic anhydride and styrene maleic acid copolymers, and the solvent medium is dimethyl sulphoxide solvent, and the electrically conducting material is copper particles and magnetic material is iron particles both essentially consisting of microsize and macrosize particles. The contraceptive is prepared by mixing the weighed quantities of copolymers and electrically conducting and magnetic materials and dissolving in dimethyl sulphoxide followed by keeping this complex solution in an inert environment and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

ESTABLISHED 1827

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RKM/IP : PCT/IN 00/00023 August 28, 2000

Copy by Fax No. : 41-22-7401435

International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Dear Sirs,

Reference : AMENDMENTS UNDER ARTICLE 19 of provisions of PCT
PCT/International Patent Application No. PCT/IN 00/00023
International Filing Date : March 16, 2000 [16/03/2000]
Priority Date : March 17, 1999 [17/03/1999]
Agent's File Reference No. IN/PA267/SKG
Applicant : GUHA, Sujoy, Kumar

The International Search Report (ISR) in respect of the International /PCT Patent application no. PCT/IN 00/00023 has been issued and mailed on 10/08/2000 by International Searching Authority (ISA) – European Patent Office (EP).

The Applicant intends to amend the claims under Article 19 of the provisions of PCT. This letter accompanies the "Amendments under Article 19" and the "Statement under Article 19(1)" of the provisions of PCT.

Amendments under Article 19 :-

Where originally there were 29 claims and after amendments of some claims there are 27 claims.

Claims 1 to 14 and claims 23 to 29 are unchanged.
Claim 17 is unchanged but amendment has necessitated renumbering as claim 15.
Claims 15 and 16 are merged and are replaced by amended claim 16.
Claims 18 and 20 are merged and are replaced by amended claim 17.
Claim 19 is unchanged but amendment has necessitated renumbering as claim 18.
Claims 21 and 22 are replaced by amended claims as claims 19 and 20 respectively.
No new claim has been added.

The claims have been amended for the first time based on the International Search Report (ISR).

The amended claims do not go beyond the disclosure of the International application as filed originally.

The amendments have necessitated retyping of originally filed pages 21 and 22. The replaced sheets 21 and 22, with claims as originally filed, duly canceled and replacement sheets 21 and 22 with amended claims are enclosed herewith.

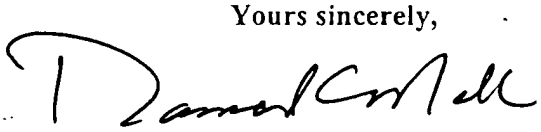
Statement under Article 19(1) :-

The Statement under Article 19(1) explaining the amendments and indicating any impact that such amendments might have on the description is enclosed on a separate sheet.

Please indicate the date of completion of technical preparation and of publication of the International Application.

The fresh Power of Attorney is enclosed.

Yours sincerely,



(Dr. Ramesh Kumar MEHTA)
Registered Indian Patent Agent
(Registration No. IN/PA-267)
PATENT AGENTS FOR THE APPLICANT
of REMFRY & SAGAR

Enclosures : Statement Under Article 19(1) – one page
Replaced Sheets nos. 21 and 22, as originally filed – two pages
Replacement Sheets nos. 21 and 22, as amended – two pages
Power of Attorney – one page
Total eight pages including two pages letter

Statement under Article 19(1)

Originally **International / PCT Patent Application [No. PCT/IN 00/00023]** had 29 claims and now, after amendments by way of merging some claims, there are 27 claims. Original claims 1 to 14 and claims 23 to 29 are unchanged. Original claim 17 and 19 are also unchanged but amendments have necessitated their renumbering as claim 15 and 18 respectively. Original claims 15 and 16 are merged and are replaced by amended claim 16. Original claims 18 and 20 are also merged and are replaced by amended claim 17. Original claims 21 and 22 are replaced by amended claims 19 and 20 respectively. No new claim has been added.

The amended claims will not have any impact on the description as the amended claims do not go beyond the scope of the originally filed patent application.

9. A contraceptive as claimed in claim 1, wherein particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 μl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claims 1 and 13, wherein said magnetic material is preferably coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body.

16. A contraceptive as claimed in claim 1, characterised in that the viscosity of the contraceptive is lowered on induction heating by an externally imposed electro-magnetic field.

17. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

18. A contraceptive as claimed in claim 1, characterised in that the contraceptive is controlled *insitu* by the application of a drag force or a propelling force by means of an external magnetic field.

19. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body.

20. A contraceptive as claimed in claim 1, characterised in that the flow of the contraceptive after injection is controlled by external means.

21. A contraceptive as claimed in claims 1 and 20, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

22. An improved injectable reversible contraceptive as claimed in claims 1 to 21 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 20 to 28 and substantially described herein above.

9. A aceptive as claimed in claim 1, whe particle size of said microsize particles of magnetic material is about 0.005 to 15μ, preferably about 0.5 to 15μ and of said macrosize particles of magnetic material is upto 0.5 mm.

10. A contraceptive as claimed in claim 1, wherein said microsize and macrosize particles of said electrically conducting material are taken approximately in equal amounts by weight.

11. A contraceptive as claimed in claim 1, wherein said microsize particles of said magnetic material are taken in lower amount as compared to said macrosize particles of said magnetic material.

12. A contraceptive as claimed in claim 1, wherein for every 100 mg of said contraceptive polymer about 200 μl of said solvent is taken.

13. A contraceptive as claimed in claim 1, wherein said magnetic material is prevented from aggregation by suitable coating.

14. A contraceptive as claimed in claims 1 and 13, wherein said magnetic material is preferably coated with cross-linked styrene maleic anhydride copolymer.

15. A contraceptive as claimed in claim 1, characterised in that the removal of the contraceptive is achieved by external magnetic field, preferably travelling magnetic field or alternately by flushing by another injection of the said solvent.

16. A contraceptive as claimed in claims 1 or 15, characterised in that the contraceptive is heated by electromagnetic induction with fields from outside the body, which in-turn causes lowering in viscosity of said contraceptive to effect the reversal thereof.

17. A contraceptive as claimed in claim 1, characterised in that the *in-situ* flow of the contraceptive after injection is controlled by external means, preferably by the application of a drag force or a propelling force by means of an external magnetic field.

18. A contraceptive as claimed in claim 1, characterised in that the presence of the contraceptive is detected and partly quantified by measuring the residual magnetic field strength from outside the body

19. A contraceptive as claimed in claims 1 or 18, characterised in that said external means include imaging by ultrasound, X-ray, CAT scan, MRI and scanning electrical impedance plethysmography.

20. An improved injectable reversible contraceptive as claimed in claims 1 to 19 and substantially described herein above.

23. A process for preparation of a contraceptive characterised by dissolving the weighed quantities of styrene maleic anhydride copolymer, styrene maleic acid copolymer, said electrically conducting material and said magnetic material in said solvent medium, preferably in dimethyl sulphoxide followed by keeping the complex solution of said copolymers, said electrically conducting material and said magnetic material in an inert environment, preferably in nitrogen atmosphere and shaking for about 45-50 hrs by maintaining the temperature at about 35^0C.

24. A process for preparation of a contraceptive, as claimed in claim 23, wherein said magnetic material is preferably coated magnetic material.

25. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are first mixed and then dissolved in said solvent.

26. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers, and said electrically conducting material and said magnetic material are directly dissolved in said solvent followed by mixing.

27. A process for preparation of a contraceptive, as claimed in claim 23, wherein said copolymers are first mixed and then dissolved in said solvent followed by addition of said electrically conducting material and said magnetic material.

28. A process for preparation of a contraceptive, as claimed in claims 23 and 27, wherein said electrically conducting material and said magnetic material are added either together or one after the other.

29. A process for preparation of a contraceptive as claimed in claims 20 to 28 and substantially described herein above.

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
MEHTA, Ramesh Kumar
Executive Consultant,FITT
Indian Institute of Technology
Dehli (IITD)
Hauz Khas, NEW DEHLI-110016
INDIA

Applicant's or agent's file reference IN/PA267/SKG	FOR FURTHER ACTION See paragraphs 1 and 4 below
International application No. PCT/IN 00/ 00023	International filing date (day/month/year) 16/03/2000
Applicant GUHA, Sujoy, Kumar	

Date of mailing (day/month/year) 10/08/2000

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designat d Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Catherine Humbert

Form PCT/ISA/220 (July 1998)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
IN/PA267/SKG		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IN00/00023	16/03/2000	17/03/1999
International Patent Classification (IPC) or national classification and IPC A61K9/10		
Applicant GUHA, Sujoy, Kumar		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 9 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
11/08/2000	18.06.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Hedegaard, A Telephone No. +49 89 2399 8644

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IN00/00023

I. Basis of the rep rt

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-7,10,13,14,16, 18,19	as originally filed	
8,9,11,12,15,17	with telefax of	26/02/2001

Claims, No.:

1,2,4-20,23-29	with telefax of	26/02/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application.

   ☒ claims Nos. 20,29.

because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

   ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 20,29 are so unclear that no meaningful opinion could be formed (*specify*):
   see separate sheet

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-2, 4-19, 23-28
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-2, 4-19, 23-28

	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-2, 4-19, 23-28
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R S ction III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. No meaningful opinion can be given for the subject-matter of claims 20 and 29 since the vague wording "substantially described herein above" renders the scope of the claims unclear (Art. 6 PCT).

Re Section V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document:

   D1: Chemical abstracts, vol. 109, no. 25 (1988-12-19) abstract no. 223418

2. The subject-matter of claims 1-2 and 4-19 is novel (Art. 33(2) PCT) since an injectable reversible contraceptive comprising (i) a contraceptive polymer from the hydrogel class of polymers, (ii) dimethyl sulphoxide solvent, (iii) an electrically conducting material which is copper in its pure form and (iv) a magnetic material which is iron in its pure form has not been disclosed in the available prior art documents.

3. The subject-matter of claims 23-28 is novel (Art. 33(2) PCT) since a process according to independent claim 23 comprising the steps of dissolving styrene maleic anhydride copolymer, styrene maleic acid copolymer, electrically conducting material and magnetic material in a solvent medium, followed by keeping the complex solution of said copolymer in an inert environment and shaking for 45-50 hrs by maintaining the temperature at 35°C has not been disclosed in any of the available prior art documents.

4. D1 (closest prior art) discloses image forming contraceptives comprising nylon, ethanol, phenol, Cu-Zn alloys and glycerol. The subject-matter of present claim 1 differs from that of D1 in specifying (i) a certain polymer, namely from the hydrogel class, (ii) a certain solvent, namely dimethyl sulphoxide, (iii) a certain electrically conducting material, namely copper in its pure form and (iv) a certain magnetic material, namely iron in its pure form.

   It could not be foreseen from D1, alone or in combination with another document, that contraceptives according to the present claim 1 would not only act as a blocking agent but brings about changes in the sperms and/or ovum. Furthermore, there is no hint in D1 to propel the contraceptives by means of an external magnetic field as is this case with the present contraceptives comprising a certain magnetic material.

   Therefore, the subject-matter of claims 1-2 and 4-19 is considered to involve an inventive step (Art. 33(3) PCT).

   The same applies mutatis mutandis to the process claims 23-28 (see however below under section VIII, item 1).

Re Section VIII

Certain observations on the international application

1. In order to keep the linking concept of the invention claim 23 should have a reference to claim 1 and the term "preferably" be deleted (Rule 13.1 PCT).

2. The words "about" and "approximately" detract from the general clarity of claims 6-10, 12 and 23 (Art. 6 PCT).

3. The claims should be renumbered due to the deleted claims 3 and 21-22 (Art. 6 PCT).

4. A discrepancy exists between independent claim 1 (iron in its pure form) and dependent claim 4 (iron in the form of oxide or a combination with a biologically accepted material); Art. 6 PCT.